DIOXIN—THE IMPACT ON HUMAN HEALTH

HEARINGS

BEFORE THE

SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT

OF THE

COMMITTEE ON SCIENCE AND TECHNOLOGY U.S. HOUSE OF REPRESENTATIVES

NINETY-EIGHTH CONGRESS

FIRST SESSION

JUNE 30; JULY 13, 28, 1983

[No. 78]

Printed for the use of the
Committee on Science and Technology

U.S. GOVERNMENT PRINTING OFFICE
32-911 O WASHINGTON : 1984

H701-52

COMMITTEE ON SCIENCE AND TECHNOLOGY

DON FUQUA, Florida, *Chairman*

ROBERT A. ROE, New Jersey
GEORGE E. BROWN, JR., California
JAMES H. SCHEUER, New York
RICHARD L. OTTINGER, New York
TOM HARKIN, Iowa
MARILYN LLOYD, Tennessee
DOUG WALGREN, Pennsylvania
DAN GLICKMAN, Kansas
ALBERT GORE, JR., Tennessee
ROBERT A. YOUNG, Missouri
HAROLD L. VOLKMER, Missouri
BILL NELSON, Florida
STAN LUNDINE, New York
RALPH M. HALL, Texas
DAVE McCURDY, Oklahoma
MERVYN M. DYMALLY, California
PAUL SIMON, Illinois
NORMAN Y. MINETA, California
RICHARD J. DURBIN, Illinois
MICHAEL A. ANDREWS, Texas
BUDDY MacKAY, Florida
TIM VALENTINE, North Carolina
HARRY M. REID, Nevada
ROBERT G. TORRICELLI, New Jersey
FREDERICK C. BOUCHER, Virginia

LARRY WINN, JR., Kansas
MANUEL LUJAN, JR., New Mexico
ROBERT S. WALKER, Pennsylvania
WILLIAM CARNEY, New York
F. JAMES SENSENBRENNER, JR., Wisconsin
JUDD GREGG, New Hampshire
RAYMOND J. McGRATH, New York
JOE SKEEN, New Mexico
CLAUDINE SCHNEIDER, Rhode Island
BILL LOWERY, California
ROD CHANDLER, Washington
HERBERT H. BATEMAN, Virginia
SHERWOOD L. BOEHLERT, New York
ALFRED A. (AL) McCANDLESS, California
TOM LEWIS, Florida

J. H. POORE, *Executive Director*
ROBERT C. KETCHAM, *General Counsel*
REGINA A. DAVIS, *Administrator*
DAVID S. JEFFERY, *Minority Staff Director*

SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT

JAMES H. SCHEUER, New York, *Chairman*

TIM VALENTINE, North Carolina
TOM HARKIN, Iowa
MICHAEL A. ANDREWS, Texas
BUDDY MacKAY, Florida
ROBERT G. TORRICELLI, New Jersey
GEORGE E. BROWN, JR., California

RAYMOND J. McGRATH, New York
CLAUDINE SCHNEIDER, Rhode Island
ROD CHANDLER, Washington
TOM LEWIS, Florida

CONTENTS

WITNESSES

	Page
June 30, 1983:	
Dr. John R. Beljan, member, Council on Scientific Affairs, American Medical Association, accompanied by Dr. Leonard D. Fenninger, vice president for medical education and scientific policy, and Harry N. Peterson, director, division of legislative activities	6
Dr. Barclay M. Shepard, Director, Agent Orange Projects Office, Department of Medicine and Surgery, Veterans Administration, accompanied by Lawrence Hobson and Maj. Alvin Young, U.S. Air Force; John Moore, D.V.M., Director, Toxics Research and Testing Program, National Institute of Environmental Health Sciences; and Dr. Vernon Houk, Director, Center for Environmental Health, Centers for Disease Control, accompanied by Dr. Renate Kimbrough, toxicologist	27
July 13, 1983:	
Dr. Sanford A. Miller, Director, Bureau of Foods, Food and Drug Administration, Public Health Service, Department of Health and Human Services, accompanied by Dr. W. Gary Flamm, Associate Director, Toxicological Sciences, Bureau of Foods, Food and Drug Administration	72
Dr. Donald Barnes, Senior Science Adviser, Office of Pesticides and Toxic Substances, Environmental Protection Agency	89
July 28, 1983:	
Dr. Irving Selikoff, director, Environmental Sciences Laboratory, Mount Sinai School of Medicine	114
Dr. Edward Brandt, Jr., Assistant Secretary for Health, Department of Health and Human Services; Dr. Vernon Houk, Director, Center for Environmental Health, Centers for Disease Control, Atlanta, Ga.; Dr. Philip Landrigan, Director, Division of Surveillance, Hazard Evaluations and Field Studies, National Institute for Occupational Safety and Health, accompanied by Dr. Marilyn Fingerhut, epidemiologist, project officer, dioxin registry studies	128
John Sommer, deputy director, National Veterans Affairs and Rehabilitation Commission, American Legion, accompanied by Paul S. Egan, deputy director, National Legislative Commission, American Legion; Lewis Milford, director, National Veterans Law Center, Washington College of Law, American University; and Maj. Gen. Murphy A. Chesney, Deputy Surgeon General, U.S. Air Force; accompanied by Maj. Jack Spey, retired, USAF, president, Ranch Hand Vietnam Association	148
Appendix: Additional material submitted for the record	183

DIOXIN—THE IMPACT ON HUMAN HEALTH

THURSDAY, JUNE 30, 1983

HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE AND TECHNOLOGY,
SUBCOMMITTEE ON NATURAL RESOURCES,
AGRICULTURE RESEARCH AND ENVIRONMENT,
Washington, D.C.

The subcommittee met, pursuant to call, at 9:30 a.m., in room 2318, Rayburn House Office Building, Hon. James H. Scheuer (chairman of the subcommittee) presiding.

Mr. SCHEUER. The subcommittee will come to order.

Today the Subcommittee on Natural Resources, Agriculture Research and Environment convenes this hearing to evaluate the available evidence on the effects of dioxin on human health. We will also examine how this evidence is being used and employed to establish the question of what levels of dioxin concentration, if any, constitute a health hazard to man.

In recent months public awareness has been heightened by disclosures of high levels of dioxin contamination at scores of locations around the country. Times Beach, Mo., and Midland, Mich., have become symbols both of the problem and the very real human suffering associated with these disclosures.

The disclosures of dioxin contamination have also raised public fears relating to exposure, whether it is by virtue of living in a dioxin-contaminated community or having been exposed to dioxin through herbicides, like agent orange, which were widely used in Southeast Asia.

The Reagan administration, if belatedly, seems to agree with the seriousness of the threat posed by dioxin contamination. It has earmarked a reported $33 million to buy Times Beach, Mo. and has obligated the Environmental Protection Agency to push forward with an intensive investigation of dioxin: how serious the threat is, how toxic it is, and the levels of dioxin contamination that are supportable and not threatening to human health.

These are significant and laudatory actions on the part of an administration generally perceived by some to be more solicitous of environmental opinions in the boardroom than on main street.

If we use the Times Beach experience as a yardstick, it is plain that repetition of the Times Beach buy-out in other areas and communities where even higher levels of dioxin have been found and become the new standard, will produce an enormously costly endeavor.

There are many of us, however, who believe that the ultimate cost in human suffering and human health problems could be even

higher if we fail to treat dioxin as the serious health threat which many responsible scientists, epidemiologists, and toxicologists believe that it well could be.

It is on this point that there seems to be confusion. Some of the confusion, in my opinion, is being deliberately engineered by those who have a vested interest stake in avoiding any findings that could establish liability for long-term health damage suffered by people exposed to dioxin.

Some of the confusion is the inevitable byproduct in the workings of a democracy of the institutional process by which a free society goes about the process of achieving consensus and making decisions and then acting on those decisions.

As we have heard in recent months, and as I presume we will hear again today, there are many people who characterize dioxin as the most toxic compound produced by man in our history; while others, such as the Dow Chemical Co., state that it produces no significant health risks; and still others, most recently the House of Delegates of the American Medical Association, who dismissed these concerns that I and others have elaborated as media hype and political posturing.

It should be pointed out that this hearing is not intended to produce a definitive answer to the exact nature and extent of dioxin-related health problems. Rather, it is our intent here to shed some light on what can and cannot be said about the effects of dioxin and to solicit recommendations on what research should be pursued to improve our understanding of dioxin and its impact on human health.

Assisting us in this task this morning will be representatives from a whole host of government agencies, and also the American Medical Association, whose 151-member house of delegates just last week voted to issue a resolution stating that dioxin does not represent a serious public health threat, as many people perceive. I am curious to hear the AMA's position in support of this position.

Finally, I would like to add a personal thought. While I don't want to put words into the mouths of my colleagues, I think I probably speak for them, too.

Nothing would give me greater pleasure than to find that the concerns I have expressed about dioxin will have proven to have been groundless by the scientific facts as they ultimately are adduced.

On the other hand, I would not like to be in the shoes of those who counsel dismissing these concerns as hysterical claptrap and media hype. They cannot afford to be wrong, and I am unwilling to have them proven wrong by doing nothing, by having this committee sit inactive and having the dioxin timebomb in our midst explode in our hands.

Before we proceed, I would like to recognize our ranking minority member of the subcommittee and a very active and contributing member of this subcommittee, Ray McGrath, for any remarks he might have.

Mr. McGRATH. Thank you, Mr. Chairman.

I am pleased that we are having this hearing today. I think it will draw attention to the seriousness of the dioxin situation and also point out directions for future research.

I wish I could just ask each of our witnesses what needs to be done in order to establish a standard for dioxin. However, I know that there are no easy answers and that there may be some serious disagreements as to the extent of the threat which may be posed by dioxin in our environment.

As some of our witnesses know, I have a dioxin problem in my own congressional district. In the town of Hempstead in New York, we have a resource recovery facility which was designed to incinerate garbage and also produce electricity. This concept was very attractive to us on Long Island because our landfills are nearing capacity.

When the plant was operating, the citizens in the area surrounding the plant—and, by the way, the horses at Roosevelt Raceway—complained of headaches, dizziness, and other symptoms. This plant has been closed for some time, both because of labor difficulties and also because it was found to emit dioxin.

Two years ago I was told by the EPA that the dioxin emitted from the stack at the Hempstead plant posed no more a threat to human health than striking a match. This year the EPA spent $30 million to buy out a town contaminated with dioxin.

More recently we have had the FDA advise the government of Michigan that 50 parts per million is the acceptable standard for fish for human consumption. Just last week the AMA announced that they didn't consider dioxin a serious threat to human health.

What becomes apparent in these instances is that there is a considerable array of opinion as to the extent of the threat from dioxin. What also becomes apparent is that we need some answers.

It seems as if every day more dioxin-contaminated sites are discovered. If more research is what is needed, then we had better make sure that it gets done. We need some answers, and we need them based on sound scientific investigation, so that we can resolve this dioxin controversy once and for all.

Mr. Chairman, I also look forward to the testimony of our witnesses. I look forward to a resolution of the problem. Thank you.

Mr. SCHEUER. Thank you, Mr. McGrath.

Now, Claudine Schneider of the State of Rhode Island.

Mrs. SCHNEIDER. Thank you, Mr. Chairman.

I, too, am most enthusiastic that we are holding these hearings today because I, like my colleagues, like my constituents, and many other people across the country, have been anxious that we could come together and discuss the health effects of the exposure to the chemical dioxin.

Some of the recent events in Missouri, Michigan, and New Jersey have almost overnight made dioxin one of the most feared of all toxic chemicals produced in this country. Unfortunately, the scientific knowledge available concerning the health effects of exposure to this substance has not kept pace with the level of public concern.

Too much of the debate over dioxin has been based upon theory and upon speculation and, quite frankly, too little upon fact and scientific evidence. Today's hearing, however, is a step toward filling the informational gap that presently exists.

I would very much like to take this opportunity to thank the witnesses in advance who have agreed to appear before this committee

today. I think your talent and your experience will be essential in determining the resources that are needed to acquire concrete answers about dioxins and about their impact on human health.

I also feel in the way of a recommendation, however, that in order to discover the truth about dioxin exposure that we ought to make this a national priority. It is unfortunate that so much of the research on the health effects seems to be disjointed and to actually lack legitimacy.

Presently we have at least five Government agencies that are involved in dioxin research. These agencies will spend more than $10 billion during fiscal year 1983 in research health effects of dioxin. I think that it is time that these agencies pooled their considerable resources and worked toward a single, authoritative analysis of the dioxin situation.

I believe that the best mechanism for coordinating and controlling this effort would be a national task force on dioxin exposure, which could be appointed by the White House and Congress and made up of a balance of experts from various Federal agencies and private groups that are presently involved in the dioxin evaluation.

A national task force made up of experts from all sides of the dioxin debate I believe is the best way to insure that future evidence on dioxin exposure will be legitimate and will be accepted. I wholeheartedly look forward to the responses of the various witnesses who we will be hearing here today upon my recommendation for a national task force and hope that we can move ahead with some resolution to this problem.

Thank you, Mr. Chairman.

Mr. SCHEUER. Thank you, Congresswoman Schneider.

The Congresswoman from Rhode Island stated a figure of $10 billion being spent researching the health effects of dioxin. I find that statement incredible. I will ask my staff to check that out during this hearing, so that we can announce whether that may have been a typographical error.

Our entire national health bill is only somewhere in the neighborhood of $300 billion. I can't believe that we are spending 3 percent of our total national health bill to research the health impact of dioxin. It is a figure that is simply not credible, and we ought to know it.

Congressman Tom Harkin of the State of Iowa, one of our most active and most contributing members.

Mr. HARKIN. Thank you very much, Mr. Chairman.

Mr. Chairman, I welcome this opportunity that you have offered today to examine the human health effects of exposure to dioxin. I thank the witnesses for coming.

Dioxin recently has been perhaps the most visible and horrifying consequence of our chemical-laden society. Each year hundreds of new chemicals appear on the market, and in many cases the only information we have on the safety of such chemicals and the contaminants from their manufacture comes from the firm that produces the chemical.

The primary Federal agency for the screening of chemicals and the protection of public health, the Environmental Protection Agency, has been paralyzed by budget cuts, mismanagement, and numerous charges of impropriety. It is difficult to estimate how

many chemicals now on the market have not been adequately screened by EPA, but the number is considerable.

While the human health effects of dioxin are the specific topic of this hearing, we must not forget that the current crisis is only a symptom of a process that allows such dangerous chemicals to proliferate.

Mr. Chairman, I also am pleased that we are having these hearings today to look into dioxin because of another aspect of dioxin that is plaguing our society. It is the effects that still linger in many of our Vietnam veterans from exposure to agent orange, which was sprayed in the jungles of Vietnam during the war.

For years we have been told that their exposure to this chemical was not harmful. Yet, I meet annually with scores of Vietnam veterans who still carry with them the effects of the exposure to tremendous amounts of this chemical sprayed as a defoliant in Vietnam.

Other studies from Great Britain, Canada, and lately from the State of Illinois show that in fact dioxin has some very subtle and very harmful effects, long-lasting effects, on the body's immunological system.

I am hopeful that these hearings will also help us to prove once and for all that our veterans who had tremendous amounts of agent orange sprayed over them in the jungles of Vietnam deserve not only to have our attention, but deserve to have their long-term illnesses addressed forthrightly by our Government; to make sure that these veterans and their spouses and their families are taken care of and are treated in every bit as efficient and humane a manner as we would if they had lost a limb in that war in Vietnam.

Mr. Chairman, again I thank you for having these hearings.

Mr. SCHEUER. Thank you very much.

Congressman Tim Valentine of North Carolina.

Mr. VALENTINE. Mr. Chairman, I don't have a formal opening statement. I would like to express my appreciation to you, Mr. Chairman, for arranging these hearings. I would like an opportunity to file a statement with the committee at the conclusion of the testimony.

Mr. SCHEUER. There being no objection, so ordered.

Congressman Rod Chandler of the State of Washington.

Mr. CHANDLER. Thank you, Mr. Chairman. I have no formal statement at this time.

Mr. SCHEUER. Very good.

We will now ask Dr. John Beljan to come to the witness table with his colleagues—they can identify themselves for the record—Dr. Leonard Fenninger and Dr. Harry Peterson.

Dr. Beljan, your entire statement will be printed in the record. I suggest that you chat with us informally, summing up your points for 7 or 8 minutes. Then I am sure we will have some questions for you.

STATEMENT OF JOHN R. BELJAN, M.D., MEMBER, COUNCIL ON SCIENTIFIC AFFAIRS, AMERICAN MEDICAL ASSOCIATION, ACCOMPANIED BY LEONARD D. FENNINGER, M.D., VICE PRESIDENT FOR MEDICAL EDUCATION AND SCIENTIFIC POLICY, AND HARRY N. PETERSON, DIRECTOR, DIVISION OF LEGISLATIVE ACTIVITIES

Dr. BELJAN. Thank you, Mr. Chairman.

First of all, I would introduce myself as John Beljan. I am a physician and eduator. I am provost and senior vice president of Wright State University in Dayton, Ohio. I am also a member of the council on scientific affairs of the American Medical Association. Mr. Chairman, if you are willing, I would be very pleased to discuss the nature and activities of the council following my comments.

I did serve as the chairman of the association's advisory panel on toxic substances that prepared the AMA's report on agent orange and dioxin contamination.

As the chairman has already noted, accompanying me today are Dr. Leonard Fenninger, who is AMA's vice president for medical education and scientific policy, and Mr. Harry N. Peterson, director of the association's division of legislative activities.

Mr. Chairman, we appreciate the opportunity to appear today to present the policy of the association concerning dioxin and its known effects on human health. We are concerned that there is a broad misunderstanding of the position of the American Medical Association, and I hope to be able to rectify that misconception this morning.

We do believe that dioxin is an important problem and an important public health problem. We have been concerned, however, with the recent news stories that have focused on areas in the country where dioxin has been found in the soil.

Physicians in Missouri, one of the sites, concerned over public reaction to the discovery of dioxin in an area in their State, brought to the AMA meeting last week in Chicago a resolution calling on the association to take action to update its December 1981 report entitled "The Health Effects of Agent Orange and Polychlorinated Dioxin Contaminants." A copy of this report is attached to this statement and I believe has been made available to your subcommittee, Mr. Chairman.

I would like to point out that on page 6 of that report, paragraph 3 begins by saying that TCDD by itself is extremely toxic. Therefore, I would like to make sure that people recognize that the AMA does, in fact, concern itself with TCDD, an extremely toxic agent, and the report which was stimulated by the problem of agent orange largely evolved into a study of dioxin.

The association was also asked to make accurate information available to the public. Specifically, the resolution that has been misquoted in the press reads as follows, and this is AMA policy:

Resolved, That the American Medical Association institute an active public information campaign to get accurate information on dioxin before the public to prevent irrational reaction and unjustified public fright and to prevent dissemination of possible erroneous information: and be it further

Resolved, That the AMA Council on Scientific Affairs be requested to update its 1981 report on dioxin.

Like you, Mr. Chairman, the AMA——

Mr. SCHEUER. Excuse me. You are only reading a short part of that. Why don't you read the "Whereas" clauses?

Dr. BELJAN. Sir, the "Whereases" are not adopted by the House as policy. The "Whereases" in a resolution being acted on by the house of delegates of the American Medical Association are very similar to a sponsor's comments when he introduces a bill or a piece of legislation. They are not part of the record; they are not part of official AMA policy. They are part of the background discussion which leads to the adoption of the resolutions, and the resolutions are the two "Resolveds" which I have just read you.

Mr. SCHEUER. I tell you, Dr. Beljan, I think you could qualify as a Philadelphia lawyer, as well as a doctor. Let me read you a couple of the "Whereases," because——

Mr. PETERSON. Mr. Chairman, may I say something, please, to just put it in perspective with what Dr. Beljan has said.

When the Congress adopts, for instance, a bill that a sponsor has introduced, the Congress does not adopt the statements of the sponsor. It adopts the language of the bill itself.

What Dr. Beljan is saying is that the two "Resolveds" that he read here are comparable to the content of the bill which a Congress may adopt.

Mr. SCHEUER. I beg to differ with you. When we pass a bill, the reasons and the underlying rationale for the bill are expressed right there in the legislation.

Mr. HARKIN. Just to back you up on that, Mr. Chairman, this is a resolution, not unlike a resolution passed by the House. When a resolution is passed by the House, all of the "Whereas" clauses are included in that resolution as it is passed by the House and Senate, whether it is a concurrent or a joint resolution. Let's set the record straight, OK?

Mr. SCHEUER. You passed this resolution——

Mr. PETERSON. Dr. Beljan said that these——

Mr. SCHEUER. Will you please stop interrupting? If you wish to be recognized, I will recognize you. When you are finished, then I will avail myself of the privilege of continuing to function as the chair of this meeting.

Would you like to continue?

Mr. PETERSON. At your pleasure, Mr. Chairman, I will be glad to——

Mr. SCHEUER. Please continue, Dr. Peterson.

Mr. PETERSON. What I was going to say is that the "Whereas," clauses are the statements of the sponsor as they have introduced the resolution. It is the formal policy of the association that when it adopts the resolution, it is adopting only the "Resolved," clauses.

Mr. SCHEUER. Let me regain my time. I really think you are being disingenuous, Dr. Peterson. This was passed as a statement to the public. This was passed as a public relations statement of the position of the AMA. It was widely printed and publicized in the press as such.

You are really being very disingenuous if you are trying to tell us the only thing that the AMA had anything to do with was the "Resolved," sentence, just one sentence. Let me read for your edifi-

cation and for the edification of everybody else here a couple of the sentences before that.

Whereas, The news media have made "dioxin" the focus of a "Witch Hunt" by disseminating rumors, hearsay and unconfirmed, unscientific reports, including quotes attributed to scientists whose quote should have been, "I don't know"; and

Whereas, The lives and well-being of many inhabitants of the regions contaminated with dioxin have been unnecessarily and ignorantly damaged by this hysterical malreporting; and

Whereas, The AMA and all members of the medical profession have a duty to speak loudly when their patients are repeatedly frightened by this wave of hysteria; therefore be it

"Resolved," and then comes your "Resolved," question.

Dr. Peterson, I have to say in all honesty that if you believe as you stated in your report 2 years ago—before the Government decided to go ahead and buy out the community of Times Beach, Mo.—October 1, 1981; if you believe, as your report said then, that dioxin by itself is extremely toxic, along with botulinus bacillus toxin and aflatoxin, that it is one of the most lethal organic chemical compounds known to man; if you believe that and you then find out that it is widely disseminated in the air, in the soil and in the water that we drink, the air that we breathe and the land that we live on, it seems to me that the AMA might well have expressed itself in a little bit more moderate terms than in the "Whereas," clauses that I just read and, indeed, in the phrase "irrational reaction and unjustified public fright" that are to be found in the very words of the "Resolved," paragraph.

It seems to me that the public had a right to be concerned. It seems to me that the Members of Congress on both sides of this aisle had not only a right but a duty to be concerned and to find out where we were in terms of research, what kind of a research design our Government agencies were carrying out and when they would be able to advise us what levels of concentration of dioxin were acceptable to human beings in the air, in the water, in food and in the human body, and what levels were tolerable now.

I don't think you could characterize that "by disseminating rumors, hearsay and unconfirmed, unscientific reports" unless you are characterizing—well, I must say I am really astonished——

Mr. MCGRATH. Mr. Chairman?

Mr. SCHEUER. I will yield to you in just a moment, Congressman.

I am astonished that a professional organization as highly respected as the AMA, with a 140-year history of high professionalism, whether you agree with every position they have taken or not, that your organization should have expressed itself in such a—well, to put it charitably, with such loose and thoughtless language.

I yield to my colleague from New York, Mr. McGrath.

Mr. MCGRATH. Mr. Chairman, whether you like the "Whereas," clauses in the resolution or not, this is not the usual way we conduct business on this particular panel. They have about 1 or 2 more pages to go of their testimony. Then if we feel constrained to beat up on them, then I think perhaps that we should. I think in all fairness we ought to let them continue their testimony and then open to question, as we do always at the end of their testimony.

Mr. SCHEUER. That would be the normal procedure.

Mr. PETERSON. Mr. Chairman, may I be recognized?

Mr. SCHEUER. Let's yield back to Dr. Beljan.

Mr. PETERSON. Mr. Chairman, may I be recognized for just a moment?

Mr. SCHEUER. Do you wish to give the testimony for the AMA?

Mr. PETERSON. No, I just wanted to respond to one question. I was asking if I could do that, Mr. Chairman.

Mr. SCHEUER. Very good.

Mr. PETERSON. That is, I go on to say very definitely and unequivocally again that the action adopted by the house of delegates are the two "Resolveds," that were read to you by Dr. Beljan and that the "Whereas," statements are statements of the sponsor of the resolution and they are not the official statements of the American Medical Association.

Mr. SCHEUER. You have said that for the record, but I think for the purposes of this hearing I will state that the entire body of that statement is the position of the AMA. It is part of their public relations posture. It was clearly released for public dissemination by the AMA. I think their statement will have to stand or fall on the basis of that one-page release.

Please continue your statement, Dr. Beljan.

Dr. BELJAN. Thank you, Mr. Chairman.

Respectfully, I would like to say that the statement that you made, sir, is AMA policy. This booklet is AMA policy. This report of the scientific council of the American Medical Association is its policy.

I would like to also say that the American Medical Association is a democratic organization and the "Whereases," are, in fact, the language of the Missouri delegation and the official policy does, in terms of the AMA conduct of its own business, become the two "Resolveds," sir.

I will stand by the report of the scientific council and would like to speak further because I do share with you, sir, the Nation's concern with dioxin as a major public health problem. But I would like to finish and then come back to that, if I may, sir.

Mr. SCHEUER. Please do.

Dr. BELJAN. We believe that the AMA has a continuing obligation to promote the public health in matters such as this and to inform the profession and the public of its most current information.

I would like to point out that before the adoption of this resolution the council on scientific affairs had determined to evaluate scientific information available subsequent to the report. This review of the new literature will take place in August. These findings are expected to be presented to the AMA board of trustees in October, with consideration by the house of delegates at its semiannual meeting in December.

Mr. Chairman, I would like to take this opportunity to highlight certain aspects of the 1981 report.

The AMA report on dioxin, which was published in 1981 and is official AMA policy, is an examination of the then available current information on the effects of the substance on animals and human health.

This study by our expert panel was a major undertaking, given the very substantial literature reporting evidence with animal and

human populations that has been generated over the past four decades.

The report recognizes the demonstrated toxicity in certain animal species of the dioxin TCDD. The report concludes that of the alleged adverse effects on human beings attributed to dioxin exposure, there is conclusive evidence of a cause and effect relationship only with respect to chloracne.

Chloracne is a not uncommon form of occupational dermatitis and may be caused by other chemical agents as well. It usually clears within several months of exposure, although severe chloracne may be persistent and has been known to last for as long as 15 years following cessation of exposure to the causal agent.

With respect to other alleged human health effects attributed to dioxin, the council on scientific affairs and its advisory panel concluded that there was insufficient published data subject to peer review to establish the relationship between dioxin exposure and the adverse health effect.

The report reviews in detail the published scientific literature that supports these conclusions. I would note that the report of the Congressional Research Service of the Library of Congress entitled "Dioxin: Environmental Impacts and Potential Human Health Effects," published June 6, 1983, surveys the body of scientific opinion and its conclusions. This survey is also consonant with the 1981 AMA report.

Mr. Chairman, the AMA strongly supports every research effort now underway examining the effects of dioxin on human beings. We are concerned that the information being made available to the public be factual information, state of the art information, be information that is not merely speculation or conjecture.

We believe very strongly that the AMA needs to continue to monitor the published studies, monitor the studies being done by our distinguished colleagues from the Federal research institutions, public and private institutions concerned with this major problem, and for us to fairly, clearly and objectively review the data as it is presented to us and to maintain our responsibilities to the practicing community and to the American public, in providing both physicians and their patients with information that is accurate and which gives us the information that we need to deal with in our interrelationships with the people we serve.

We do not feel that we have sufficient information in a number of areas. There are suggestions of concerns, and we intend to review these as a scientific panel. That scientific panel will operate independently, objectively and conscientiously and will update its report based on the evidence available to us, which we have reviewed in the interim, since the report in 1981, and try to bring up to date the official policy of the AMA, which is reflected in this booklet, and to resolve.

Thank you, sir.

[The prepared statement and report of Dr. Beljan follow:]

STATEMENT

of the

AMERICAN MEDICAL ASSOCIATION

to the

Subcommittee on Natural Resources, Agriculture
Research and Environment
Committee on Science and Technology
U.S. House of Representatives

Presented by
John R. Beljan, M.D.

Re: Dioxin

June 30, 1983

Mr. Chairman and Members of the Subcommittee

My name is John R. Beljan, M.D. I am Provost and Senior Vice-President of Wright State University in Dayton, Ohio. I am currently a member of the Council on Scientific Affairs of the American Medical Association. I served as chairman of the Association's Advisory Panel on Toxic Substances that prepared the AMA's report on "Agent Orange" and dioxin contamination. Accompanying me are Leonard D. Fenninger, M.D., AMA's Vice President for Medical Education and Scientific Policy, and Harry N. Peterson, Director of the Association's Division of Legislative Activities.

Mr. Chairman, the AMA appreciates the opportunity to appear today to present the policy of the Association concerning dioxin (TCDD) and its known effects on human health.

Recent news stories have focused on areas in this country where dioxin has been found in the soil. Physicians in Missouri, one of the sites, concerned over the public reaction to the discovery of dioxin in an area, brought to the AMA meeting last week in Chicago a resolution calling on the Association to take action to update its December 1981 report entitled "The Health Effects of 'Agent Orange' and Polychlorinated Dioxin Contaminants." A copy of this report is attached to this statement. The Association was also asked to make accurate information available to the public. Specifically, the resolution reads:

> RESOLVED, That the American Medical Association institute an active public information campaign to get accurate information on dioxin before the public to prevent irrational reaction and unjustified public fright and to prevent dissemination of possible erroneous information: and be it further
>
> RESOLVED, That the AMA Council on Scientific Affairs be requested to update its 1981 report on dioxin.

The AMA has a continuing obligation to promote the public health in matters such as this and to inform the profession and the public of the most current information. I would like to point out that before the adoption of this resolution, the Council on Scientific Affairs had determined to evaluate scientific information available subsequent to the report. This review of the new literature will take place in August. The findings are expected to be presented to the AMA Board of Trustees in October with consideration by the House of Delegates at its meeting in December.

Mr. Chairman, I would like to take this opportunity to highlight certain aspects of the 1981 report.

The AMA report on dioxin is an examination of the then available current information on the effects of the substance on animals and human health. This study by our expert panel was a major undertaking given the very substantial amount of literature reporting experience with animal and human populations that has been generated over the last four decades. The report recognizes the demonstrated toxicity in certain animal species of the dioxin TCDD when it is ingested. The report concludes that of the alleged adverse health effects on human beings attributed to dioxin exposure, there is conclusive evidence of a cause and effect relationship only with respect to chloracne. Chloracne is a not uncommon form of occupational dermatitis and may be caused by other chemical agents. It usually clears within several months of exposure, although severe chloracne may be persistent and has been known to last for as long as 15 years following cessation of exposure to the causal agent.

With respect to other alleged human health effects attributed to dioxin, the Council on Scientific Affairs and its advisory panel concluded that there was insufficient published data subject to peer review to establish a relationship between dioxin exposure and the adverse health effect. The report reviews in detail the published scientific literature that supports these conclusions. I would note that the report of the Congressional Research Service of the Library of Congress entitled, "Dioxin: Environmental Impacts and Potential Human Health Effects," published June 6, 1983, surveys the body of scientific opinion and its conclusions. This survey is consonant with the 1981 AMA report.

Mr. Chairman, the AMA strongly supports every research effort now underway examining the effects of dioxin on human beings.

At this time, we will be pleased to respond to any questions the Subcommittee may have.

32-911 O—84——2

AMERICAN MEDICAL ASSOCIATION HOUSE OF DELEGATES

Resolution: 12
(A-83)

Introduced by: Missouri Delegation

Subject: Education of Public Regarding Dioxin

Referred to: Reference Committee E
(Raymond Scalettar, M. D., Chairman)

Whereas, "Dioxin" occurs in many forms, some non-toxic and another said to be the most powerful toxin known to man; and

Whereas, The dioxin form 2, 3, 7, 8 TCDD is highly toxic to guinea pigs and variably much less so to other species of lab animals; and

Whereas, This form of dioxin can be found contaminating soils and waters in varying degrees in parts of the United States; and

Whereas, An AMA study (Report A of Council on Scientific Affairs, I-81) has not found any documented human deaths directly attributable to dioxin poisoning, and very little morbidity; and

Whereas, From the same study it is evident that no one knows or can truthfully say what level of body dioxin or environmental dioxin is dangerous to humans; and

Whereas, The news media have made "dioxin" the focus of a "Witch Hunt" by disseminating rumors, hearsay and unconfirmed, unscientific reports, including quotes attributed to scientists whose quote should have been, "I don't know"; and

Whereas, The lives and well-being of many inhabitants of the regions contaminated with dioxin have been unnecessarily and ignorantly damaged by this hysterical maireporting; and

Whereas, The AMA and all the members of the medical profession have a duty to speak loudly when their patients are repeatedly frightened by this wave of hysteria; therefore be it

RESOLVED, That the American Medical Association institute an active public information campaign to get accurate information on dioxin before the public to prevent irrational reaction and unjustified public fright and to prevent dissemination of possible erroneous information; and be it further

RESOLVED, That the AMA Council on Scientific Affairs be requested to update its 1981 report on dioxin.

Past House Action: I-81: 176-179

Mr. SCHEUER. Dr. Beljan, I can't disagree with a word that you have just said. We, too, are concerned with the lack of definitive scientific evidence. That is why we are here. I don't suppose there is a subcommittee in the Congress that has pressed more eagerly and more insistently for the Federal Government to proceed with better research, a higher quality of scientific research, on the question of dioxin and dioxin's effects on human health than this subcommittee.

We are not satisfied with the current data base which scientists, on the one hand, or Government regulators, on the other hand, have to work with. I couldn't disagree with a sentence or a syllable that you have expressed. I congratulate you for the thoughtful, measured phrases which you have used in expressing yourself.

I must say that there is a dramatic inconsistency between the sense of what you are saying and the sense of the 1981 report, which is quite consistent with the message you have given us, and the sense of this document.

Dr. BELJAN. We regret some of the imprudent language of our Missouri colleagues, sir.

Mr. SCHEUER. Why don't we leave it at that? I respect your testimony and I respect the remark you have just made.

First, I am going to yield to a Member of Congress who is not a member of this committee, the distinguished Member of Congress from Pennsylvania, Mr. Tom Ridge, who is a Vietnam war veteran and who is very much interested in agent orange and dioxin.

Tom Ridge of Pennsylvania.

Mr. RIDGE. Mr. Chairman, I want to thank you very much for the courtesy that you have extended to me, and Congresswoman Schneider, for sitting in as an observer and occasional participant today as time permits.

There are, to my knowledge, 50 or 60 Vietnam-era veterans in Congress but there are, I believe, a dozen Vietnam theater veterans who serve in the House of Representatives. I am proud and privileged to be among that group.

Obviously, as an infantry soldier I have a particular interest in the kind of research that is being conducted not so much personally, because if I can believe the information we have, it was not used in the particular area that I was located, but I have many friends involved in other parts of the country where I think it was used.

Again, thank you very much for this opportunity to sit in and participate. If not formally, I will probably send out some questions of my own, with the chairman's permission.

Mr. SCHEUER. Very good.

Mr. RIDGE. Thank you, sir.

Mr. SCHEUER. Thank you very much for joining us.

Claudine Schneider.

Mrs. SCHNEIDER. Thank you, Mr. Chairman.

Dr. Beljan, the question has been raised that the original sponsor of the resolution, Dr. George Bohigian of Washington University in St. Louis, Mo., might have had a vested interest in introducing this resolution insofar as the university has received considerable financial support, to the tune of $30 million, from Monsanto Co., a company which has been associated with some dioxin contamination.

I think it is important that we raise this question early on in these hearings. I would like some of your comments on that.

Dr. BELJAN. I wonder if I might speak to the nature of the Council on Scientific Affairs because I think it is important to the context of this hearing.

The Council on Scientific Affairs was established 6 or 8 years ago in order to provide for the AMA an objective source within its own structure for its important mission of information review and conveyance to its members.

It is a council which consists of 12 members, elected from the constituency on a rotating basis, nominated by the constituency, and represent, we would like to think, reasonable people who believe they have an important obligation to provide valid scientific information.

We are not all experts in our own field. Therefore, we constitute a variety of advisory committees, of which each member of the council normally serves as a liaison, hence my involvement with this particular committee.

We attempt to provide through that mechanism national experts who can address the question, can provide a definitive statement, who may or may not be AMA members, who may or may not be physicians, but who are recognized for their scientific expertise.

That report as they constitute it is then reviewed by the full council on scientific affairs and is then presented to the house of delegates through the board of trustees for adoption as scientific policy of the AMA.

We believe that we have a very creditable record with our membership and with the American public. We would like to continue that.

We also believe that research is an important key to finding some of the answers today of the problem of dioxin. Research does not happen by itself. It requires funding, and it requires funding from a variety of sources.

Mrs. SCHNEIDER. Well, I wonder if you could—I appreciate your clarifying the bureaucracy of the AMA for me. It sounds about as complex as our own.

Dr. BELJAN. I think it is very important because it functions as a quasi-autonomous body within a structure that has been known for a long time as rather paternal and protective. It is willing to call a spade a spade.

Coming to your specific question, in order for us to review research objectively and completely we need to have that research done. That research is supported by the Federal Government, it is supported by private industry, it is supported by foundations, it is supported by individuals.

We do not see an inherent conflict of interest necessarily with the source of funding and the work being carried out. I would believe that Dr. Bohigian and St. Louis University will conduct their research program in a true, objective, scientific approach.

Mrs. SCHNEIDER. Was Mr. Bohigian the chairman of the research council within your bureaucracy? Did he have any title role in the AMA?

Dr. BELJAN. He has just been elected to the council on scientific affairs.

Mrs. SCHNEIDER. But he was one of many members of the council on scientific affairs.

Dr. BELJAN. He has just been elected. He is coming in to fill a vacancy.

Mrs. SCHNEIDER. I see. That council is made up of doctors from all across the United States?

Dr. BELJAN. Pardon me, ma'am?

Mrs. SCHNEIDER. The council is made up of doctors from all across the United States?

Dr. BELJAN. Yes, plus a medical student and a student physician in training, selected by their peer groups.

Mrs. SCHNEIDER. I still can't help but think that there is an awful lot of coincidence here, that he is newly appointed to the council and he is the one who initiates a report that shows less than real caution or public concern. I know most of my constituents were appalled to see the kind of attitude that was projected by the AMA as a result of what was going on with dioxin.

I am curious to know, once you pass a resolution, do the doctors who have conducted the research on the human health effects of dioxin have to have membership on the council, the doctors who have done the research?

Dr. BELJAN. No.

Mrs. SCHNEIDER. That is not necessary.

Dr. BELJAN. No. We will do that through our advisory committee, which is the group that originally drafted this report, which was then adopted by the council and the house.

Mrs. SCHNEIDER. Was this resolution reviewed by the membership of the AMA?

Dr. BELJAN. This was done through the process of the reference committee, has gone through the State structure and was brought to the house of delegates, was reviewed in the reference committee and was brought to the floor on a consent calendar. But again, the operating philosophy is that the "Resolveds," are the parts that become AMA policy, not the preamble.

Mrs. SCHNEIDER. I understood that in your opening remarks. What I was curious about is what is the normal procedure for the resolutions to be reviewed by the AMA membership?

Dr. BELJAN. The normal procedure is that these come through the State organization, are brought to the AMA at its house by the State delegate, is assigned to a reference committee, which then reviews these and makes recommendations to the House regarding adoption, again, of the resolution, not the "Whereases,".

Mrs. SCHNEIDER. So, was this particular resolution according to your traditional procedures?

Dr. BELJAN. Yes.

Mrs. SCHNEIDER. It was?

Dr. BELJAN. Yes.

Mr. SCHEUER. Will my colleague yield?

Mrs. SCHNEIDER. Yes, I would be happy to yield.

Mr. SCHEUER. I find it hard to understand as a practical matter how such egregiously intemperate and ill-considered language could possibly have worked its way through whatever screening processes you have, so all of a sudden it could appear in the big

wide world out there and before press, media, congressional committees, television as AMA policy.

If one of my 14 year old kids wrote such an intemperate, irresponsible, demagogic editorial in a high school newspaper, I would be embarrassed by it, and I would whack their fannies.

How could this have gone through your screening process, so that this now, this piece of paper represents the considered policy and the considered consensus of 300,000 doctors in the United States? It boggles the mind.

Dr. BELJAN. Mr. Chairman, may I respond, please?

Mr. SCHEUER. Please do.

Dr. BELJAN. Again, I seem to be hitting at the same point, but it is an open process.

Mr. SCHEUER. Open is putting it mildly. It is out of control if something like this can end up before the——

Dr. BELJAN. Not so, sir, because the two resolutions are constant with AMA policy, which is this, which was also adopted by action of the house of delegates.

Mr. SCHEUER. To make our feeling clear, that document that you just held up is a prudent, thoughtful statement that I don't see how anybody could take exception to, dated October 1, 1981. You are bringing that up to date. You just said this morning that you hoped we would accrue more knowledge so that we could fine-tune our judgments about dioxin. Absolutely unexceptionable.

This piece of paper is totally inconsistent with your words this morning and with that October 1, 1981 document. I am absolutely dumbstruck at how it could ever have gone through all of your processes and ended up here before the klieg lights.

Mr. PETERSON. Mr. Chairman, may I be recognized?

Mr. SCHEUER. I think we have really exhausted your sentiments on the subject. I really would like to hear from Dr. Beljan.

Mr. PETERSON. I would like to be heard, if possible. I would only be a very brief moment.

Mr. SCHEUER. Could I please let Dr. Beljan finish?

Mr. PETERSON. May I say something when he is finished, then?

Mr. SCHEUER. Of course.

Mr. PETERSON. Thank you very much.

Dr. BELJAN. I can understand your consternation. We are concerned at times with the language of our peers. I believe even Congress has been known to use imprudent language on occasions.

The official policy does call for——

Mr. SCHEUER. Let me say we do use imprudent language from time to time, but we have some very excellent machinery from preventing silly things from happening around here. We have a committee process, the subcommittee process, the hearing process, the floor process, then it is the conference process and the Senate process. We don't generally act in silly ways. You may not agree with everything that we do, but we have a very terrific, fine, finely tuned screening process.

Dr. BELJAN. The point I am trying to make, Mr. Chairman, is that this resolution in its form could have just as easily been not adopted but could have raised the same kind of concern about the language.

That is a product from Missouri. I think we could all talk about how we feel about that. However, I think it is important to recognize that there are two very important pieces in this that are now AMA policy; that is, that the AMA Council on Scientific Affairs get about the business of updating this important report and hopefully to continue to provide this kind of very sound, sensible statement of where we are in the scientific literature and, second, to disseminate this kind of information and hopefully to encourage the public to accept information in its factual form rather than its conjectural form.

Mr. SCHEUER. Dr. Beljan, I am going to yield back to my colleague, Mrs. Schneider.

Mr. PETERSON. Mr. Chairman, may I remind you that I was to have an opportunity of speaking following Dr. Beljan.

Mrs. SCHNEIDER. I would be happy to hear from you, Dr. Peterson, now that I have regained my time.

Mr. PETERSON. May I also correct the record. Thank you very much, but it is not Dr. Peterson. I am not a physician.

I would like to say that I don't think the Chair is suggesting that the AMA should have a censorship mechanism with respect to its membership. I would hope that that is not what is being suggested here.

I would say that the screening process that the Chair has indicated is the same process that the AMA has as it hears the resolutions. The resolution is introduced by a sponsor, it is referred to a committee, it is heard by the membership, it is discussed, it is debated, the reference committee makes its report, just as the committee of the Congress does, but the reference committee reports the words of the "Resolved."

Again, I want to say that the screening process that evolves then results in the "Resolveds," that were adopted, so that the screening process took this resolution and the screening resulted in the "Resolveds," just as he described the congressional process.

Thank you.

Mrs. SCHNEIDER. Thank you very much. We have a large number of members here who are most anxious to ask some questions. I would just like to very quickly ask my final question, which moves from the procedure on to content. It is probably a question that not only my constituents but all the people across the country are anxious to have an answer on.

That is, as you are putting together—part of your "Resolved," says that your council on scientific affairs is going to update your report on dioxin. You say that we do not have sufficient information.

My question is when? When are we going to have some type of definitive statement? I recognize that it is difficult for scientists to be too definitive at any one time, but when are we going to have some idea of what the safe levels of human exposure to dioxin might be?

Dr. BELJAN. I think you are correct that it is impossible to answer that question.

Mrs. SCHNEIDER. I won't let you off the hook that easily.

Dr. BELJAN. I understand.

Mrs. SCHNEIDER. If we could have an idea. Certainly your report must have some time element to it, that you are anxious to have it in print by *x* date.

Dr. BELJAN. Understand that the council will update its report on the presently available literature. I think your question is best posed to our Federal colleagues who will succeed us in testimony this morning.

Mrs. SCHNEIDER. I will ask this question to all witnesses.

Dr. BELJAN. They are going to be doing some very important work that is central to the question you asked. There is also some information which permits us to make some statements, but they don't resolve the kinds of questions that you need to address as policymakers. We are sensitive to that fact. The association would like to be helpful in that regard, but we cannot fabricate data. We can only interpret the data from our scientific community.

Mrs. SCHNEIDER. I would think that the AMA would feel that the onus is upon them, after having come out with a statement that more or less pooh-poohs the whole dioxin situation, and put full speed ahead on coming forward with some type of scientific report that we can use in conjunction with the report that might be put forward by EPA or by Monsanto or by whatever other entities are also doing the research.

Dr. BELJAN. Please, may I put the matter to rest that the AMA does not pooh-pooh dioxin. I as a responsible medical educator believe very strongly that we have a major public health problem with dioxin. That is the policy of the AMA.

We need to get more information, we need to sponsor and encourage research geared at this, but the problem is complex. Dioxin itself is one of a family of compounds. There are 22 isomers of dioxin. There are 50-odd members of that family. There is a related chemical structure, a family very similar to it. The material behaves very strangely in earth. We don't know its bioviability. We don't know human loads.

There is a wealth of information that demands answering before one can give you the kind of data you need to have.

Mr. SCHEUER. The gentlelady's time has expired.

Mrs. SCHNEIDER. Thank you.

Mr. SCHEUER. Congressman Tom Harkin of Iowa.

Mr. HARKIN. Thank you very much, Mr. Chairman.

Dr. Beljan, just to go over it one more time for as much clarity as I can elicit, on the review committee that reviewed this statement, was there anyone or can you tell me how many on this review committee had any knowledge or experience at all in dioxin research?

Dr. BELJAN. My sense would be that the majority of the panel had some relationship to dioxin research, some more and some less, but I believe all are individuals who are conversant with the problem of dioxin, and particularly our respected scientists can appreciate the scientific method.

Mr. HARKIN. I am sorry, the respected scientists who?

Dr. BELJAN. Who can utilize the scientific method, see data and review it effectively.

Mr. HARKIN. Was this the panel that reviewed it? There is a panel that is listed in this brown book that you said is the official statement.

Dr. BELJAN. That is correct. That is the panel that wrote the draft paper that was then reviewed by the council on scientific affairs.

Mr. HARKIN. So this panel that is in this book that published this booklet on agent orange/dioxin a couple of years ago is the same review committee that reviewed the statement that we have been discussing?

Dr. BELJAN. That is not correct, sir. I am sorry.

Mr. HARKIN. What I am asking you is about this statement that was issued. It was referred to reference committee E, Raymond Scalettar, M.D., chairman. This is the committee that approved this statement, right?

Dr. BELJAN. The reference committee approved the "Resolveds."

Mr. HARKIN. The reference committee approved the "Resolveds."

Dr. BELJAN. That is correct.

Mr. HARKIN. Who approved the "Whereases," that came out in this?

Dr. BELJAN. The Missouri delegation and the discussion of the group, but there was never formal approval of the "Whereases."

Mr. HARKIN. All right. Then let me ask you this. Did the AMA then in any way seek to correct the impressions that the press disseminated throughout the United States that this was indeed not the position of the AMA and it was only the position of a small group of delegates from the State of Missouri?

Dr. BELJAN. May I refer that to my colleague from the AMA?

Dr. FENNINGER. Mr. Chairman, we have had numerous inquiries from the press. We have done our best to make clear that during the process of the reference committee, the reference committee in its wisdom saw fit to eliminate all of the language that had been introduced by the Missouri delegation, for the very reasons that you have raised; namely, that it was not germane to getting on with the problem of getting evidence and disseminating evidence about the dioxin problem, particularly TCDD, and that it did not represent AMA policy.

Therefore, the reference committee in its hearings did not report any of those "Whereases," to the house of delegates. We have repeatedly said this to the press and explained, as we have here, what the process is.

Mr. HARKIN. Excuse me, Dr. Fenninger. Let me ask you then, this piece of paper that I have is titled "American Medical Association House of Delegates, Resolution: 12." On the bottom it says, "Past House Action: 1-81: 176-179." What does that mean?

Dr. FENNINGER. That does refer to this particular report on scientific affairs. That is a note that there has been a previous House action related to the dioxin question.

Mr. HARKIN. That is that booklet that was put out?

Dr. FENNINGER. Yes.

Mr. HARKIN. But you are saying that this one here, which is resolution 12, that all of the "Whereas," clauses were never approved by the AMA?

Dr. FENNINGER. That is correct.

Mr. HARKIN. Again, I just say, did you do anything to dispel this in the press? I just refer to a front page story in the New York

Times of June 25 called the debate over dioxin. Let me read you one paragraph, to show you the impact that this has had.

> President Reagan became the latest to join the fray when he suggested Thursday in his news conference that news reports about dioxin "have frightened a good number of people unnecessarily." He was reacting to a resolution approved Wednesday by the American Medical Association that condemned the news media for conducting a "witch hunt" against dioxin, thus generating "unjustified public fright" and "hysteria".

So even the President of the United States believes that the AMA has said that. Would you please so inform the President that you have not said that?

Dr. FENNINGER. Yes, sir.

Mr. HARKIN. That would tend to clear it up. I accept what you say is true. If so, then the AMA has been done a great injustice here. Things are being said and quoting you in which you ought not to be quoted as saying. I hope the AMA would come out with a very strong statement saying this is not so.

Is there any possibility of the AMA taking such a step to correct the record on this?

Mr. PETERSON. May I respond to that and just indicate that I hope the matter has been explained satisfactorily to the committee. I think the difficulty that we had initially to get that message across here is compounded in trying to get that message across to the press. We will certainly do everything that we can, and we are doing everything that we can to explain that to the press.

Mr. HARKIN. Mr. Peterson, have you ever issued a press statement clarifying it? If you do, could we have a copy of it for our record? Have you? I see a nodding of a head. No, I see someone shaking their head.

Dr. BELJAN. Sir, there has not been a written statement, but our director of communications assures us that there have been 75 individual media contacts since this resolution became publicly aware refuting the fact that this is official AMA policy.

Mr. HARKIN. Why hasn't the AMA—Dr. Beljan, you are the president of the AMA, are you not?

Dr. BELJAN. Negative, sir.

Mr. HARKIN. What are you?

Dr. BELJAN. I am simply a humble member of the council on scientific affairs, representing my association, which is the AMA.

Mr. HARKIN. Mr. Chairman, perhaps we ought to have the head of the AMA up here to find out why they have not issued a statement to the press. If there has been 75 individuals, I would think the AMA would come out with a statement.

Mr. PETERSON. May I say this, that in addition to the various individual contacts I am advised that there would be no problem in issuing a general press release. We would be very happy to have that forwarded.

Mr. HARKIN. Let me ask you this. Do you intend to issue a statement to the press clarifying this and stating quite emphatically what you have just stated for us, that these "Whereases," are not part of AMA policy?

Mr. PETERSON. There would be no problem, sir.

Mr. HARKIN. And you will do that, to clarify it once and for all?

Dr. BELJAN. Yes, sir.

Mr. HARKIN. Thank you very much.

Mr. SCHEUER. Thank you.

Congressman McGrath of New York.

Mr. MCGRATH. Thank you, Mr. Chairman.

May I just point out that I would hope, as the chairman said, that at the next house of delegates meeting the "Whereases," would be more temperate and also point out to the chairman that if he wants to see some demagogic and intemperate statements, all he has to do is look at the extension of remarks in the record every day.

I am interested in the composition of the council on scientific affairs. Does it conduct its own research or does it just compile and review research done by others and then come to some conclusion?

Dr. BELJAN. It is primarily the latter. Where there is a particular problem that we believe is important to bring a state-of-the-art message to our membership or to the public, we will then constitute a special advisory panel of experts to do that, working on behalf of the council on scientific affairs.

Mr. MCGRATH. In the compilation and review and conclusion process of all of the dioxin research held up to this point in time, you have concluded that chloracne is the only direct result of dioxin contamination at this point in time?

Dr. BELJAN. It is, to our best opinion, the only direct causal relationship that we believe is proved. There are other associations, there is further data on some of the associations, but that has not been proved to our satisfaction.

Mr. MCGRATH. Do you believe that the resultant exposure to dioxin is a cumulative process, that the more you are exposed to it the more apt you are to have some sort of a reaction, or do you believe that one or two incidents of being exposed to dioxin is enough to cause a carcinogenic or any kind of reaction?

Dr. BELJAN. I would not like to be conjectural, but we do know that with most toxins, and I would suspect TCDD being one of them, that there are two phenomena that one would see in acute exposure or chronic exposure. I would expect to see different effects from large doses of each.

Mr. MCGRATH. Finally, just to reiterate a question that was asked previously, when do you expect to update your report on dioxin?

Dr. BELJAN. We will update our report beginning really next month by reassembling this advisory panel.

Mr. MCGRATH. How many new scientific studies are you going to review in the compilation of this new report?

Dr. BELJAN. There are a series of studies in progress, the information from which we will review: the Air Force Ranch Hand study, the Armed Forces Institute of Pathology study. We would like to see some of the VA data. We would like the association to develop an opportunity to review the latest information from CDC because we believe that it is in the public's best interest and the profession's best interest to have available to us the most current, latest information.

Mr. MCGRATH. Incidentally, how many studies were reviewed in order to come up with this document?

Dr. BELJAN. The published papers are several hundred. Many of them are different viewpoints of the same study. Some are critical analyses. Others are less critical. But in essence, we reviewed the ful literature available at the time. We will again do the full literature at this time and hopefully have shared with us other information that may as yet be unpublished.

Mr. MCGRATH. Thank you.

Mr. SCHEUER. Congressman Torricelli.

Mr. TORRICELLI. Thank you, Mr. Chairman.

Sir, I represent a State that is now going through the trauma of a dioxin problem, New Jersey. We read with interest and concern that Times Beach, with an exposure level of 500, created considerable concern; Newark, with a level of 1,200 in some areas; then in Clifton we were told that it was safe with levels of 11, yet we have read the Centers for Disease Control talks about a level of 1.

What exactly are you advising the doctors of America is a level of concern? At what point should communities react with a degree of concern and a feeling of danger?

Dr. BELJAN. We are not giving physicians an absolute level that we have with confidence. That is one of our dilemmas. We would like to be able to provide that kind of information. So, I cannot answer that question in terms——

Mr. TORRICELLI. You don't feel that at this point any of these levels can be accepted? The contradiction here is I have reports of a man in 1979 being hospitalized for exposure to 50 parts and yet people are now being told in other areas that greater levels seem safe. In fact, you do not feel comfortable in assessing any level?

Dr. BELJAN. I believe one can be comfortable in assessing extremes of level. When you ask me the question what are some of the break points or thresholds or this kind of data, we simply do not have the data. I don't believe anyone has the data. It is our hope that some of the work that is in progress and yet to be done will give us some information that will shed some light on making some reasonable estimates of what these threshold levels are.

Mr. TORRICELLI. I read with interest, in following the Hooker Chemical episode, that when they were charged that a level of 10 was dangerous to the population in parts per trillion, they did not argue and seemed to accept that that was a dangerous level and that it was dangerous to the health of people in that community. They might have had some regrets after they read the AMA statement that perhaps even they were too concerned with public health.

Did they not have accurate information, either? Were they just accepting something falsely that they should not have, in fact, responded to?

Dr. BELJAN. I have no relationship with Hooker, and I have no access to the information on which they made that decision. I cannot make or would not be willing to conjecture on that decision.

Mr. TORRICELLI. Let me ask you a final question. This is to general AMA policy.

Generally, as one individual with absolutely no medical background, when I am exposed or involved or ingesting a drug or chemical that I don't understand, and I don't know its results on

my body, my rule of thumb is don't allow exposure, maximum concern, don't allow myself to become involved with it.

The opinion of the AMA seems to be exactly the opposite. If you don't understand it and there isn't any evidence to say that it is wrong, don't become concerned about it and it is a witch hunt.

Is my rule of thumb for myself, that I won't allow myself and would be concerned about any levels of exposure, something that I don't understand? Does that mean I am on a personal witch hunt?

Dr. BELJAN. I regret the unfortunate continuing use of the word "witch hunt." Again, that is not AMA policy.

Mr. TORRICELLI. What I am really getting at—and I don't want to create a difficult situation for you—is in general, when you advise doctors about concerns on chemicals or exposure levels, isn't the better rule if you don't understand it, if there isn't enough evidence, maximum concern, raise public alarm, not lower it? Isn't that the real point?

Dr. BELJAN. Let me say the approach should be conservative, but I think you have already hit on what we need to do; that is, we need to look at the individual situation. We need to look at the concentrations involved, the individual, the individual's predilections and susceptibilities, their age, debilities, state of health. We need to look at the exposures, the route of administration.

It is very difficult for me to be able to give you some broad statements. Obviously threshold levels, the one part per billion being established as a recommendation by the CDC is obviously a very conservative number and is based on their best estimate of some projections, and I will listen with interest in how they derived that.

When you are talking about a part per billion, that is the reverse of the Federal deficit in terms of magnitude. It is an extremely small quantity.

Mr. TORRICELLI. This is a difficult enough discussion without bringing the deficit into it.

Dr. BELJAN. Respectfully, sir, I can't answer your question in the framework in which it is posed.

Mr. TORRICELLI. I was suggesting if that isn't just generally a better approach, because we are going to run into these problems in the future as well.

Dr. BELJAN. We believe the conservative approach is better, too, sir, yes.

Mr. TORRICELLI. I also wanted to join my colleague from Indiana in that obviously there is a need here now for AMA to have a massive public relations campaign to reverse some damage.

There are people all across America now concluding that the principal worry of dioxin is acne. That is of enormous concern, I know, to the adolescents in my State, but it is making everyone else rest easy when they should be vigilant in their action and concern.

I hope, in fact, you will do your best to reverse an enormous misconception on this population that could lead to real danger because people will not insist that the laws be enforced and that sites be cleaned and will not seek the medical help that they should be seeking.

Thank you.

Mr. SCHEUER. Thank you.

Congressman Tom Lewis of the State of Florida.

Mr. LEWIS. Thank you, Mr. Chairman.

Dr. Beljan, I have a little bit of concern. The animals that are showing the effects of dioxin in the laboratories are the same type of animals that we use to test other types of toxicants and things of this nature.

Don't you show some concern that they are reacting to this compound?

Dr. BELJAN. Absolutely we have concern about it. That is why we believe that the agent is a very toxic agent. The problem is how can one translate animal data to man. The problem is the individual susceptibility of various kinds of animals to this particular agent. There are members of the rodent family that differ by factors of 500 in their susceptibility to the lethality of the agent.

There is no question that in a variety of animal studies this compound does show dramatic effects. It shows carcinogenesis, the creation of cancers and tumors. It does show other various serious problems. The problem is how does one then extrapolate that to man.

Man appears to be relatively less susceptible. There is no good correlation for this particular compound between some other primates and man as a primate. We are concerned, yes, but we cannot establish levels, dosage levels, or some of the causal relations.

Mr. LEWIS. I have one further question, Mr. Chairman.

Dr. John Quinson with the Pesticide Research Center in Michigan State University has been performing laboratory experiments to identify certain types of bacteria that will actually eat dioxin. Are you familiar with this?

Dr. BELJAN. I know of it in general.

Mr. LEWIS. Do you think this is a program that AMA would support in order to eliminate any of the dioxin questions?

Dr. BELJAN. We will support research in any endeavor that shows promise of addressing the dioxin problem. One of the problems with dioxin, particularly in soil, is its inability to be degraded. One of the approaches to that might very well be bacterial or microbiological.

Mr. LEWIS. Thank you, Doctor.

Thank you, Mr. Chairman.

Mr. SCHEUER. Thank you, Tom.

Congressman Tom Harkin for one brief additional question.

Mr. HARKIN. Just one short question, Dr. Beljan.

There was a study conducted by Dr. Milford Ward of the Department of Immunology, Royal Hallenshire Hospital, Sheffield, England, which documented a long-term immune system breakdown in humans exposed to dioxin some 10 years prior to their examination.

Are you aware of this study? Has your committee looked at it?

Dr. BELJAN. I am personally not aware of the study. We have not looked at it in detail at this point.

Mr. HARKIN. I recommend that you do take a look at it and let us know what you think of that study.

Thank you.

Dr. FENNINGER. Mr. Chairman, may I have permission for a word?

Mr. SCHEUER. Very briefly, because we must make this rollcall vote.

Dr. FENNINGER. We think that this is a very important hearing. We believe that important information will come out of the hearing that will be useful to our council on scientific affairs. We look forward to having information from all sources and working with governmental and nongovernmental agencies and organizations in the resolution of this serious social and potentially serious health problem.

Thank you.

Mr. SCHEUER. Thank you very much. We thank this panel for its patience. We are going to adjourn this hearing for about 10 or 12 minutes, until we make this rollcall vote. Immediately when we get back we will convene the next panel.

The hearing is suspended.

[Recess.]

Mr. SCHEUER. The subcommittee will come to order.

We will invite the panel to join us at the committee table: Dr. Barclay Shepard, Dr. Young, Dr. Moore, Dr. Houk, and Dr. Kimbrough.

What we will ask each of you to do—we have a large panel—is to speak for 5 or 6 minutes, summing up your testimony. All of your testimonies will be printed in full in the record. After you have chatted with us, then we will have questions at the end of all of your comments.

We will start with Dr. Barclay Shepard, Director of the Agent Orange Program at the Veterans' Administration. Please proceed, Dr. Shepard.

STATEMENTS OF BARCLAY M. SHEPARD, M.D., DIRECTOR, AGENT ORANGE PROJECTS OFFICE, DEPARTMENT OF MEDICINE AND SURGERY, VETERANS' ADMINISTRATION, ACCOMPANIED BY LAWRENCE HOBSON AND MAJ. ALVIN YOUNG, U.S. AIR FORCE; JOHN MOORE, D.V.M., DIRECTOR, TOXICS RESEARCH AND TESTING PROGRAM, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES; AND VERNON HOUK, M.D., DIRECTOR, CENTER FOR ENVIRONMENTAL HEALTH, CENTERS FOR DISEASE CONTROL, ACCOMPANIED BY RENATE KIMBROUGH, M.D., TOXICOLOGIST

Dr. SHEPARD. Mr. Chairman and members of the committee, we are pleased to have the opportunity to appear before this committee to discuss VA research efforts on the health effects of exposure to dioxin.

I am Dr. Barclay Shepard, Director of the Agent Orange Projects Office of the VA's Department of Medicine and Surgery. With me this morning are two very able members of my staff, Dr. Lawrence Hobson——

Mr. SCHEUER. Dr. Shepard, you will not have time to read your 13-page statement.

Dr. SHEPARD. This is a summary, sir.

Mr. SCHEUER. Very good. Please proceed.

Dr. SHEPARD [continuing]. Dr. Lawrence Hobson, and beside me Major Alvin Young, Ph. D., U.S. Air Force.

Dr. Hobson has had a distinguished career in the VA, having served as Deputy Assistant Chief Medical Director for Research and Development. He has a strong background in medical research and pharmacology.

Dr. Alvin Young, on detail from the Air Force to the VA, is certainly one of the world's experts on the chemistry, physiology and various uses of herbicides, especially those used for military purposes in Vietnam.

I would like to briefly summarize my statement and submit my full statement for the record.

The VA's research efforts in this area are focused on answering the many questions and concerns of Vietnam veterans who may have been exposed to dioxin as a consequence of the spraying in Vietnam of the defoliant agent orange.

The VA and others are engaged in an extensive research program to assure that we find answers to the scientific and medical questions surrounding such exposure. Research studies in this country and abroad have begun to provide pertinent information.

We foresee that these and other well-planned, carefully executed studies will enable us to provide scientifically acceptable answers to whether or not exposure to dioxin plays a significant role in the development of disease.

The scientific process on which these studies must be based is necessarily exacting and time consuming. We would stress that while awaiting the results of these scientific inquiries the VA is providing a broad range of health care benefits to Vietnam veterans who believe that they have experienced health problems related to agent orange exposure.

Most of the herbicide agent orange was deposited from aircraft on jungle foliage, where much of the dioxin was degraded by exposure to ultraviolate light. However, certainly some dioxin did enter soil and water.

These circumstances have made it difficult to estimate how much contact any one veteran has had with dioxin and poses a major problem in attempts to determine what health effects dioxin may have produced in veterans.

The VA has undertaken or supported several major studies as a part of a coordinated Federal effort to evaluate the possible health effects of exposure to the phenoxy herbicides.

The VA has undertaken a major mortality study to analyze and compare mortality patterns and specific causes of death of veterans who served in Vietnam as contrasted to comparable veterans who did not.

VA researchers are currently in the process of examining information contained in the records of 60,000 veterans who have died following military service during the Vietnam era. This important study is well underway, and we anticipate that publication of results should occur by December of 1984.

The Vietnam veteran twin study, another important research effort, involves the comparison of identical twin veterans, one of whom served in Vietnam during the period of agent orange spraying and the sibling who did not serve in Southeast Asia. This study will examine up to 500 pairs of twins using psychological, physio-

logical and biochemical tests to measure the impact, if any, of service in Vietnam.

Since 1970, the Environmental Protection Agency has been collecting human adipose tissue from a statistically representative segment of the general population. Among approximately 4,000 tissue specimens available for chemical analysis, there are tissues from 555 males of the Vietnam veteran age group. Many of these individuals will have served in the military during the Vietnam era, and some will have served in Vietnam during the period of agent orange use.

Under an interagency agreement between VA and EPA, we will assay these tissue samples to determine the background levels of dioxin and furans in the U.S. male population. We will also determine whether service in the military, and especially in Vietnam, has had an effect on these values. The assays are both exacting and lengthy. Accordingly, we do not expect final results until 1985.

Public Law 96-151 directed the design and conduct of an epidemiological study of Vietnam veterans who were exposed to dioxins contained in herbicides, including agent orange. The VA and the Department of Health and Human Services have executed an interagency agreement that provides that the Centers for Disease Control will design and conduct this important epidemiological study.

The CDC has distributed their protocol for evaluation by a number of groups. The study will examine the effects of exposure to agent orange as well as determine if there are any adverse health effects of Vietnam and the service in general.

The Centers for Disease Control is also conducting a birth defect study to determine if Vietnam veterans have a higher than expected risk of having children with birth defects. The study is jointly funded by the VA, the Department of Defense, and the Department of Health and Human Services. We understand the CDC expects to complete the study in early 1984.

In addition, two international studies have been reported within the last few months. Australian scientists examined records from 34 hospitals and 4 cytogenetic laboratories to identify infants with birth defects and a matched group of healthy infants to serve as controls. In all, approximately 8,500 children were involved in the study.

The fathers of infants with birth defects and the fathers of the controls were identified and their service in the Australian army was determined, as well as their duty in Vietnam. The study found no evidence that service in Vietnam increased the risk of fathering a child with a birth defect.

Researchers in New Zealand conducted a study of 981 professional sprayers and a control group of unexposed agricultural contractors to determine the number of births, congenital defects, and miscarriages among the families of these groups.

There was no statistically significant difference between the number of birth defects and miscarriages in the two groups. In addition, exposure of the wives had no detectable reproductive effect.

In late 1981 the VA issued a solicitation letter requesting VA scientists to submit research proposals to examine the biochemical,

physiological, or toxicological aspects of herbicides and dioxin exposure.

Our Medical Research Service has approved and funded 10 new research studies that investigate the impact of low levels of exposure to the ingredients of agent orange, including dioxin, on basic biological processes.

These studies include an analysis of the effects of the components on agent orange on liver cell function, on neuro-behavioral functions, and the biochemistry of chloracne. The results of these studies should be available in the next year or so.

Chloracne, as you have heard, is a skin disease which has been linked to exposure to dioxins and certain other chlorine containing compounds. A task force of VA dermatologists is charged with evaluating skin conditions in Vietnam veterans, coordinating special examinations of certain veterans, developing a special examination for questionable cases, and preparing a monograph on chloracne.

A special review of some 3,200 cases by Vietnam veterans who sought compensation for conditions claimed to be due to exposure to agent orange identified some 300 cases where the conditions described might suggest chloracne.

Of these 14 men, 13 were examined at 1 of 3 prestigious, non-VA clinics. The remaining veteran, although located, has not been examined due to his remote job location. None of the 13 veterans examined to date was diagnosed as having chloracne, although one man gave a history of exposure and a subsequent skin problem that is compatible with chloracne.

Several studies carried out in foreign countries, most notably studies conducted in Sweden, have suggested a possible association between exposure to phenoxy herbicides and subsequent development of soft tissue sarcomas, a group of relatively rare malignant tumors. Other international studies failed to confirm the existence of this association.

The first VA effort in this area involves a survey of the records of Vietnam-era patients treated in VA hospitals with a diagnosis of soft tissue sarcoma. The preliminary review indicates that service in Vietnam does not materially increase the risk of developing soft tissue sarcoma.

The second VA effort in this area is a special soft tissue sarcoma study which will be accomplished in cooperation with the Armed Forces Institute of Pathology. This study will use the AFIP registry of soft tissue sarcomas, one of the largest and most consistently accurate in the world, to provide cases among males of the Vietnam veteran age group.

This study is designed to determine whether veterans who served in Vietnam have a higher risk of developing this type of tumor than those who did not.

Mr. Chairman, many questions remain unanswered with respect to the health effects of dioxin. The current research will not answer them all. You, sir, have asked for our opinion on what additional research needs to be done.

One of the most pressing issues for the VA and for the other groups concerned with this issue is the question of bioavailability of dioxin in various environments; in other words, what is the like-

lihood that dioxin can adversely affect humans and animals when exposure occurs in different ways.

We know, for example, that dioxin under some circumstances becomes very tightly bound to carbon and other elements in the soil. We need to know to what extent dioxin is bound and whether the body can remove it from these various materials.

In order to evaluate this risk, we need much more information about how the human body handles dioxin. Additional studies designed to explore the biological behavior of these substances are needed to determine how dioxin is absorbed, distributed within the body, altered, destroyed, or excreted.

Of course, extensive research on animals must continue to precede any attempts to study humans. However, it may be possible in the future to conduct safe and useful studies of humans using state-of-the-art scientific methods. In the meantime, most information on the human health effects must come from continued epidemiological studies of people exposed during industrial and other operations.

The Veterans' Administration shall continue to support in every way we can the research needed to provide answers to the puzzling questions related to the concerns of the public at large, as well as and especially the concerns of the veterans whom we serve.

Mr. Chairman, this concludes my statement. I will be happy to answer any questions you may have.

[The prepared statement of Dr. Shepard follows:]

STATEMENT OF

BARCLAY M. SHEPARD, M.D.

DIRECTOR, AGENT ORANGE PROJECTS OFFICE

DEPARTMENT OF MEDICINE AND SURGERY

VETERANS ADMINISTRATION

BEFORE THE SUBCOMMITTEE ON

NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT

COMMITTEE ON SCIENCE AND TECHNOLOGY

UNITED STATES HOUSE OF REPRESENTATIVES

JUNE 30, 1983

Mr. Chairman and Members of the Committee:

Good morning. We are pleased to have the opportunity to appear before this Committee to discuss VA research on the health effects of exposure to dioxin, the current state of knowledge concerning such exposure and associated health effects. The VA's research efforts in this area are focused on answering the many questions and concerns of Vietnam veterans who may have been exposed to dioxins as a consequence of the spraying in Vietnam of the defoliant "Agent Orange".

The VA is keenly aware of the depth of the public and veterans' concerns over this subject and is engaged in a multi-faceted scientific research effort to resolve the issue. The VA, and others, are engaged in this extensive

research program to assure that we find answers to the scientific and medical questions surrounding such exposure. Research studies in this country and abroad have begun to provide pertinent information. We foresee that these and other well-planned, carefully executed studies will enable us to provide scientifically acceptable answers to whether or not exposure to dioxin plays a significant role in the development of disease or other disorders.

We would stress that we are approaching these questions with dedication, objectivity, and a commitment to achieving scientific validity. The scientific process on which these studies must be based is necessarily exacting and time consuming. We would also stress that while awaiting the results of these scientific inquiries, the VA is providing a broad range of health care benefits to Vietnam veterans who believe they have experienced health problems related to Agent Orange exposure.

Agent Orange was a mixture of equal parts of two phenoxy herbicides, 2,4-D and 2,4,5-T. The latter contained a very small amount, averaging 2 parts per million, of the dioxin 2,3,7,8-TCDD as a contaminant which appeared during the manufacturing process.

Agent Orange was sprayed from fixed-wing aircraft, helicopters, trucks, boats, and back packs primarily to remove broadleaf foliage that served as cover for the enemy. Most of the herbicide was deposited on jungle foliage where the dioxin was rapidly degraded by exposure to ultra-violet light. Some dioxin did reach the soil and entered water, both standing and running.

These circumstances have made it difficult to estimate how much contact any one veteran has had with dioxin. Indeed the estimation of exposure poses a major problem in attempts to determine what health effects, if any, dioxin may have produced in veterans.

RESEARCH

The VA has undertaken or supported several major studies as part of a coordinated federal effort to evaluate the possible health effects of exposure to the phenoxy herbicides. Permit me to outline the current status of those studies.

Vietnam Veteran Mortality Study:

In the conduct of any large scale survey which examines the health effects of chemical or other environmental agents, an essestial element is an examination of mortality data.

A carefully designed and well-executed mortality analysis of Vietnam veterans would provide answers to questions raised by the Agent Orange exposure issue, in particular, and the possible health effects of service in Vietnam, in general. Accordingly, the VA has undertaken the Vietnam Veteran Mortality Study to analyze and compare mortality patterns and specific causes of death of veterans who served in Vietnam as contrasted to comparable veterans who did not. VA researchers are currently in the process of examining information contained in the records of 60,000 veterans who have died following military service during the Vietnam era.

The data-gathering phase of this important study is well underway and we anticipate that data collection will be completed by March 1984. Data analysis, final review, and publication of results should occur by December 1984.

Vietnam Veteran Twin Study:

The Vietnam Veteran Identical Twin Study involves a comparison of identical twin veterans, one of whom served in Vietnam during the period of Agent Orange spraying, and the sibling who did not serve in Southeast Asia. This study will examine up to 500 pairs of twins, using psychological, physiological, and biochemical tests to measure the impact, if any, of service in Vietnam. Differences in results within the twin pairs will be examined as a function of both service in Vietnam and exposure to the dioxin-containing herbicide.

We anticipate the development of a final protocol within the next three to four months. Completion of the study depends upon our success in locating and recruiting participants. We anticipate the final results of this study in two to three years. We would stress, however, that this study will provide the most sensitive means we can devise for detecting any subtle effects of Vietnam service.

Dioxin/Furan Adipose Tissue Study:

In a limited study conducted in 1979-1980, the VA found that dioxin, or TCDD, could be detected and quantified in adipose tissue removed from Vietnam-era veterans. Although no clear relationship was found between levels of TCDD and Vietnam

service, exposure to Agent Orange, or current health status, the study suggested a need for further investigation.

Since 1970, the Environmental Protection Agency has been collecting human adipose tissue from a statistically representative segment of the general population and analyzing it for residues of selected pesticides and polychlorinated biphenyls (PCB's). Among approximately 4,000 tissue specimens available for further chemical analysis, there are tissues from 555 males born between 1937 and 1952. Many of these individuals will have served in the military during the Vietnam-era, and some will have served in Vietnam during the period of Agent Orange use. Under an interagency agreement between VA and EPA, we will assay these tissue samples to determine the background levels of dioxins and furans in the U.S. male population. We will also determine whether service in the military, and especially in Vietnam, has had an effect on this value. The assays are both exacting and lengthy. Accordingly, we do not expect final results until 1985.

The study itself has three phases. In a first phase, researchers will contact hospital pathologists to further identify the tissue donors and then determine their service status from their military records. The second phase involves developing analytic methods for determining selected

dioxins and furans in human adipose tissue and subjecting that methodology to rigorous independent validation. The last phase is the tissue analysis itself and preparation of a final report.

We have already begun to obtain the military and occupational histories of the 555 men and are in the process of designing a uniform method of analyzing dioxin levels in fat.

Epidemiological Study of Agent Orange:

Public Law 96-151 directed the VA to design and conduct an epidemioogical study of Vietnam veterans who were exposed to dioxins contained in herbicides including Agent Orange. Efforts to develop a protocol revealed the difficulties in determining who had been exposed to Agent Orange in Vietnam, and who had not. Initially, it seemed that such a determination would be virtually impossible, but diligent efforts by the Army Agent Orange Task Force, have now made it likely that groups or cohorts of exposed and unexposed Vietnam veterans can be identified.

The VA and the Department of Health and Human Services have executed an interagency agreement that provides that the Centers for Disease Control will design and conduct this epidemiological study.

The CDC has distributed their protocol for evaluation by several groups. It calls for three parallel studies, one to examine the long-term health effects of exposure to herbicides and dioxins, one to determine if there are any adverse health effects of Vietnam service in general, and one to determine the risk of soft-tissue sarcomas and lymphoma among Vietnam veterans.

CDC Birth Defects Study:

In addition to the epidemiology study, the Centers for Disease Control is conducting a birth defects study in the Atlanta, Georgia, area where subjects have been identified through the CDC's Metropolitan Congenital Defects Surveillance Program. The study is jointly funded by the VA, the Department of Defense, and the Department of Health and Human Services. We understand that CDC expects to complete the study in early 1984. In addition, two international studies have been reported within the past few months.

In their Birth Defects Study, "Case Control Study of Congenital Anomalies and Vietnam Service Birth Defects Study", Australian scientists examined records from 34 hospitals and four cytogenetic laboratories to identify infants with birth defects. Matched healthy infants born in the same hospitals served as controls. In all approximately 8,500 children were involved in the study. The fathers of the infants with birth

defects and the fathers of the controls were identified and their service in the Australian Army was determined as well as their duty in Vietnam. The study as reported found no evidence that service in Vietnam increased the risk of fathering a child with a birth defect.

In New Zealand, the manufacture and spraying of phenoxy herbicides, including those contaminated with dioxin, have exposed many workers to these chemicals. Both sprayers and their wives are exposed during field spraying and handling of herbicides. Researchers in New Zealand conducted a study entitled "Congenital Defects and Miscarriages Among New Zealand 2,4,5-T Sprayers." This was a survey of 981 professional sprayers and a control group of unexposed agricultural contractors to determine the number of births, congenital defects, and miscarriages among the families of both groups. There was no statistically significant difference between the numbers of birth defects and miscarriages in the two groups. In addition, exposure of the wives had no detectable reproductive effect.

VA Specially Solicited Research Projects:

In late 1981 the VA issued a solicitation letter requesting VA scientists to submit research proposals to examine the biochemical, physiological, or toxicological aspects of herbicide and dioxin exposure. During fiscal year 1982, our

Medical Research Service approved, and in fiscal year 1983 funded, 10 new research studies that investigate the impact of low levels of exposure to the ingredients of Agent Orange, including dioxin, on basic biological processes. These studies include an analysis of the effects of the components of Agent Orange on liver cell function, on neuro-behavioral functions, and the biochemistry of chloracne. The results of these studies should be available in 1985 and 1986.

Chloracne Review:

A Chloracne Task Force of VA dermatologists is charged with reviewing and evaluating skin conditions resembling chloracne, coordinating special examinations of veterans with questionable skin conditions, developing a chloracne examination protocol, and preparing a monograph on chloracne.

A special review of some 3,200 claims by Vietnam veterans who sought compensation for conditions claimed to be due to exposure to Agent Orange identified some 300 cases where the conditions described might suggest chloracne. A VA dermatologist then reviewed the medical records of the 300 claimants and identified 14 veterans who could have chloracne. Of these 14 men, 13 were examined at one of three prestigious non-VA clinics. Each received a complete medical

examination, including a special dermatological evaluation. The remaining veteran, although located, has not yet been examined due to his remote job location. None of the 13 veterans examined was diagnosed as having chloracne although one man gave a history of exposure and a subsequent skin problem that is compatible with chloracne.

Soft-Tissue Sarcoma Studies:

The VA has initiated two efforts to determine whether there is a relationship between service in Vietnam and the subsequent development of soft-tissue sarcomas. Several studies carried out in foreign countries, most notably studies conducted in Sweden, have indicated a possible association between exposure to phenoxy herbicides and subsequent development of soft-tissue sarcomas. Other international studies failed to confirm the existence of this association.

The first VA effort in this area involves a survey of the records of Vietnam-era veteran patients discharged from VA hospitals with a diagnosis of soft-tissue sarcoma. The results of this survey are still being analyzed but the preliminary review indicates that service in Vietnam does not increase the risk of developing soft-tissue sarcoma. There was also no single type of sarcoma that characterized the tumors among Vietnam veterans.

The second VA effort in this area is a special soft-tissue sarcoma study which will be accomplished in cooperation with the Armed Forces Institute of Pathology. This study will use the AFIP register of soft-tissue sarcomas, one of the largest and most consistently accurate in the world, to provide cases among males of the Vietnam veteran age group. Their veteran status will be obtained from their military records. This study is designed to determine whether veterans who served in Vietnam have a higher risk of developing this type of tumor than those who did not.

Future Research:

Many questions remain unanswered with respect to the health effects of dioxin. The current research will not answer them all.

The most pressing issue for the VA and for the other agencies concerned with this issue seems to us to be that of the bioavailability of dioxins in various environments. In other words, what is the likelihood that dioxin can adversely affect humans and animals when exposure occurs in different ways? We know, for example, that dioxin under some circumstances becomes tightly bound to carbon and other

elements in soil. Soils, however, vary and so do other materials in contact with dioxin in the environment. We badly need to know the extent to which dioxin is bound and whether the body can remove it from various materials. Only when we know the extent of this bioavailability can we evaluate the risk of dioxin in our environment.

In order to evaluate this risk, we need much more information about how the body--the human body--handles dioxin. Additional studies designed to explore the biological behavior of these substances are needed to determine how dioxin is absorbed, distributed within the body, altered or destroyed and excreted. Of course, extensive research on animals must precede any attempt to study humans. However it may be possible in the future to conduct safe and useful studies of humans, using state-of-the-art scientific methods.

In the meantime, most information on humans must come from continuing epidemiological studies of people exposed during industrial operations. The Veterans Administration shall continue to support in every way we can the research needed to provide answers to the puzzling questions related to the concerns of the public as well as the veterans whom we serve.

Mr. SCHEUER. Thank you very much, Dr. Shepard. We will hear all the witnesses and then we will ask questions of all the witnesses. Indeed, the witnesses at that point can ask questions of each other. I think that will be a good process.

Now we will hear from Dr. Moore, if you will take your 6 or 7 minutes, then we will hear from Dr. Houk, and then we will have questions.

Please proceed, Dr. Moore.

Dr. MOORE. I am pleased to appear before you today to discuss aspects of dioxin health effects from a scientific perspective. As a toxicologist, I have conducted and directed research on this chemical and have consulted or served on committees dealing with public health aspects of TCDD.

I would like, Mr. Chairman, to highlight a couple of things in my testimony. I think the rest of it will have already been said before the hearing is over, as far as the known data.

While there are human data that document the immediate or short-term effects of TCDD exposure, the long-term sequela is not as well understood. There is a body of data dealing with carcinogenic effects of TCDD that is disquieting. Several studies in Sweden report an association between exposure to TCDD or phenoxy acids and an increased risk of soft tissue sarcoma. Several animal studies also predict human carcinogenic hazard.

Some of the earliest and perhaps the most severe human exposures occurred in industrial settings. Findings derived from these accidents are of potential value in confirming cancer risks. Because they occurred long ago, cancers could be emerging in the current timeframe based on that exposure.

However, by virtue of the sample size involved in a number of these exposures, there is a very real limit to the power of these various studies to detect an increased cancer risk, if indeed it was there.

There are two studies underway to enhance the sample size associated with industrial exposure: The U.S. Dioxin Registry, being conducted by the National Institute of Occupational Safety and Health, and the International Dioxin Registry, being coordinated by the International Agency for Research on Cancer.

Recent events in several States demonstrate that there are TCDD contaminated environments to which the public may be exposed and that the number of contaminated sites being detected is increasing.

It has been observed that TCDD has a natural tendency to bind to components of soil. Some scientists speculate that in such an instance the toxicity potential may well be diminished.

If TCDD bioavailability is appreciably diminished due to binding of soil, it may have practical utility in assessing risk associated with given levels in the environment. A series of experiments are currently in progress at my institute to study the bioavailability of TCDD.

I can stop here, Mr. Chairman.

[The prepared statement of Dr. Moore follows:]

STATEMENT BY JOHN A. MOORE, D.V.M.

Mr. Chairman and Members of the Subcommittee: I am pleased to appear before you today and discuss aspects of dioxin (2,3,7,8 tetrachlorodibenzo-p-dioxin or TCDD) health effects from a scientific perspective. As a toxicologist, I have conducted and directed research on this chemical and have consulted or served on committees dealing with public health aspects of TCDD.

The toxicity of TCDD in animals has been evaluated using conventional pharmacological and toxicological procedures. Because of its biological potency, TCDD has also been employed extensively as a model toxin in a variety of basic research toxicologic studies including mutagenesis, carcinogenesis and teratogenesis studies. We have learned that, in general, TCDD produces a characteristic pattern of short-term toxic effects which involve skin, liver and the immune system in animals. In addition, when administered to pregnant animals, TCDD can cause fetal toxicity and fetal death. However, it does not appear that exposure to TCDD produces adverse genetic effects, alters fertility in male rodents, or increases the incidence of malformed offspring sired by treated males. Several independent studies in experimental animals have also revealed that TCDD is carcinogenic. In addition, two separate laboratory research techniques have shown that TCDD is a potent promoter of chemically-induced cancer. The biological potency of this chemical has intrigued scientists and continues to stimulate research into the mechanism by which it produces its effect(s). I will now discuss selected aspects of TCDD toxicity from the viewpoint of human hazard as it relates to known animal effects.

It is accepted that human exposure to 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD) can produce a skin disease called chloracne. Observations made following the accident in Seveso, Italy have confirmed that chloracne is a definitive human indicator of TCDD exposure. The severity and duration of chloracne are variable; those exposed in the Seveso accident generally evidenced transient effects. In contrast, the chloracne developing in some workers exposed to TCDD in an accident which occurred in 1949 has persisted for as long as 30 years. The differing time course probably reflects variation in degree and duration of exposure. The Seveso incident and some other industrial accidents have also revealed that liver toxicity may be a consequence of TCDD exposure. Thus in terms of effects on skin and liver, the results of animal toxicity studies correlate with the human data.

Animal studies have clearly demonstrated that TCDD may affect components of the immune system. The very young appear to be most susceptible; while low doses of TCDD may stimulate immune function, higher doses produce immunosuppression—a phenomenon also seen with other chemicals. It has been reported that studies of immune function in Seveso children with chloracne revealed either no effect or a mild stimulation. If these data are correct (they need independent review), one may speculate that chloracne is an earlier sign of acute TCDD toxicity than is immune depression. Draft reports of immunological studies of English workers industrially exposed to TCDD remain unpublished, unconfirmed, and report incomplete data. Thus interpretation of the reported findings is not possible.

Another stated concern is that TCDD exposure may cause decreased fertility and an increase in the number of children with birth defects. An extensive study involving male mice that were exposed to high levels of TCDD, 2,4,5-T and 2,4-D failed to demonstrate a decrease in fertility or an increase in malformed offspring. These data, plus knowledge that TCDD is not considered to be a mutagen, fail to support the hypothesis that males exposed to TCDD are at an increased risk of fathering malformed children. The current U.S. Air Force Study of the men who applied Herbicide Orange, and who were therefore potentially exposed to TCDD, is evaluating their fertility and the incidence of birth defects in their children.

There is clear laboratory evidence that TCDD exposure of pregnant rodents can produce embryotoxic and embryolethal effects, and TCDD has been reported to produce renal malformations and cleft palate in laboratory mice. These experimental data suggest that TCDD exposure may pose a reproductive hazard in women. There has been little, if any, evidence of an increase in the incidence of spontaneous abortions, congenital malformations or postnatal effects following the Seveso accident. However, there is a paucity of acceptable data currently available to address this point, and a cohort epidemiologic study of women exposed to TCDD would provide valuable information. The design and execution of such a study is a formidable challenge given the inherent limitations of a small number of subjects, "spontaneous" 4% incidence of major birth defects diagnosed during the first year of life and the fact that 20–30% of "normal" conceptions do not result in live births.

Drawing on the data that I have cited, there is reason to believe animal studies are of value in predicting the nature of the toxicity associated with TCDD exposure.

In my opinion, the major limitation in extrapolating laboratory knowledge of TCDD to man is the wide range of doses required to produce an effect. Because of the varying susceptibilities of different animal species, the dose required to produce a toxic effect varies several thousand fold. The major priority should be to conduct studies that relate dose to the human toxicological or biological response and the stability or decrease in the TCDD body burden over time.

While there are human data that document the immediate or short-term effects of TCDD exposure, the long-term sequelae are not as well understood. There is a body of data dealing with carcinogenic potential of TCDD that is disquieting. Several studies in Sweden report an association between exposure to TCDD or phenoxyacids and an increased risk of soft tissue sarcoma or lymphoma in humans; several animal studies also predict human carcinogenic hazard. Some of the earliest and perhaps the most severe human exposures occurred in industrial settings; findings derived from these accidents are of potential value in confirming cancer risk because they occurred long enough ago that cancers resulting from the exposures would now be emerging. Several recent publications report the health findings or cause of death in some of these populations, but each, by virtue of sample size, is limited in its power to detect increases in specific diseases. Two studies are underway to enhance the sample size associated with industrial exposure—the U.S. Dioxin Registry being conducted by the National Institute for Occupational Safety and Health and the International Dioxin Registry being coordinated by the International Agency for Research on Cancer, WHO with funding provided by the National Institute of Environmental Health Sciences (NIEHS).

Recent events in Missouri, Michigan and New Jersey demonstrate that there are TCDD contaminated environments to which the public may be exposed and that the number of contaminated sites being detected is increasing. It has been observed that TCDD has a natural tendency to bind to components of soil. Some scientists speculate that in such an instance the toxicity potential would be diminished. If TCDD bioavailability is appreciably diminished due to binding in soil, it may have practical utility in assessing risk associated with levels in the environment. A series of experiments are currently in progress at NIEHS to study TCDD bioavailability from soil.

As final point, I wish to alert the committee that the "dioxin" we all refer to is but one member of a chemical family. There are other members of this family that have also been demonstrated to have toxic and carcinogenic potential. Members of another closely related family of chemicals, the chlorinated dibenzofurans, are frequently found as contaminants in products that contain dioxins. The pattern of disease that the other toxic dioxins and dibenzofurans produce is indistinguishable from the observed with TCDD. Basic research with these chemicals indicates that a common mechanism is probably involved in their toxicity. Therefore, the public health risk should be assessed by calculating aggregate exposure to all of these chemicals, not only to TCDD.

I would be pleased to answer any questions the committee may have.

Mr. SCHEUER. Dr. Houk?

Dr. HOUK. Thank you, Mr. Chairman, and members of the subcommittee.

I am Dr. Vernon Houk, also a physician, Director of the Center for Environmental Health, Centers for Disease Control, Public Health Service, Atlanta. I am accompanied by Dr. Renate Kimbrough, a toxicologist on my staff, who I might add is well recognized in the international community as one of the preeminent toxicologists in this area and in the world.

I am pleased to be here this morning in response to your request for testimony on the health effects of dioxin. It is important to recognize that there are 75 related compounds generally referred to as dioxin.

My testimony relates specifically to the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin, or TCDD, the most toxic. I will attempt to summarize what is known and can provide for the record a brief scientific overview, including pertinent literature citations. [Detailed responses to subcommittee questions on dioxin to be submitted at a later date.] Most of the information on health effects

comes from extensive animal studies and some studies of workers exposed to dioxin-containing products.

It is generally agreed that dioxin can cause chloracne. In addition, porphyria cutanea tarda, an acquired form of porphyria characterized by chronic skin lesions and other symptoms, has been observed in some instances after dioxin exposure.

Industrial workers inadvertently exposed to dioxin have complained of weight loss, easy fatigability, aching muscles, insomnia, irritability and loss of libido, but these complaints are very difficult to evaluate. Also, after such exposure, abnormal liver function tests have been reported in association with tender liver and liver enlargement.

Neurological changes in sensory function have been observed. There is evidence that there may be an association between workers exposed to dioxin-containing products and soft tissue sarcoma. This latter is particularly important since soft tissue sarcomas have been observed by the National Toxicology Program in mice exposed through the skin to dioxin.

The human health effects of dioxin in relation to long-term exposure to dioxin in either high or low dose are not known since adequate studies have not been done, and I would like to emphasize that.

In animal studies, TCDD has been shown to be a very toxic compound for many species of animals. The acute lethal dose varies widely but is as low as 0.6 micrograms per kilogram in guinea pigs.

Various forms of tumors have been shown in different species, as have liver abnormalities, porphyria, abnormalities in the immune system, especially of immature animals, birth defects in mice and general toxic effects on fetuses of other species when females are fed and injected with dioxin during the period of conception.

The only male animal study for birth defects was done in mice and did not demonstrate any birth defects when the male was fed, during the mating period, simulated agent orange contaminated with dioxin.

A great deal of research on the health effects of dioxin is underway. It is very difficult to quantify exposure in humans. The CDC birth defects study may be able to determine whether there is an association between birth defects in children and service of their fathers in Vietnam where they may have been exposed to agent orange.

The epidemiology studies of the veteran population and the soft tissue sarcoma component of that study will be used to determine whether health effects have occurred in these populations.

Careful epidemiologic studies are needed in part because of differences between the Swedish studies that report increased risks of soft tissue sarcoma and other international studies which, as conducted and reported—I would like to emphasize that, also—fail to confirm this association.

CDC's NIOSH is completing a registry of workers exposed to dioxin-containing products. That registry will include 6,000 workers and will be used for information on death and its cause and on illness among those workers.

The Veterans' Administration is looking at the mortality among the Vietnam veterans, whether there is a difference in identical

twins exposed in Vietnam, and other facets. CDC is also studying the effects on people who have been exposed to dioxin in soil in the United States. These studies are just beginning. It is difficult to predict what any of these studies will tell us.

One problem with all of the studies is that one cannot determine the actual dose of dioxin that an individual received. Therefore, misclassification of people into exposure groups could occur and lead to erroneous results.

For example, it would be possible to include in a single group people who absorbed varying amounts of dioxin with people who did not absorb any dioxin. Since it would be clearly unethical to administer dioxin to humans, we may need to continue to look at animal data as a factor in making predictions about toxic effects of dioxin on humans.

There is no doubt that considerable additional research will need to be done. Some of it can be identified now. Some will become obvious as results from studies already undertaken become available and as we have more experience with inadvertent exposures either when they occur or at some point after a continuous exposure, such as happened in Missouri.

I would suggest that further studies in the following areas are needed: uptake and bioavailability of dioxin from different soils and the development of better methods for determining the amount of dioxin in the body and a better understanding of the mechanism of action of dioxin in the animal model.

Mr. Chairman, that concludes my formal remarks. Dr. Kimbrough and I will be happy to answer any questions you or other members may have.

Thank you.

[The prepared statement of Dr. Houk follows:]

TESTIMONY BY DR. VERNON N. HOUK

Mr. Chairman and members of the Subcommittee:

I am Dr. Vernon N. Houk, Director, Center for Environmental Health, Centers for Disease Control (CDC), Public Health Service, Atlanta, Georgia. I am accompanied by Dr. Renate Kimbrough, a toxicologist on my staff.

I am pleased to be here this morning in response to your request for testimony on the health effects of dioxin and to address the questions you specifically asked. It is important to recognize that there are 75 related compounds generally referred to as dioxin. My testimony relates specifically to the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). I will attempt to summarize what is known and can provide for the record a brief scientific overview including pertinent literature citations.

Most of the information on health effects comes from extensive animal studies and some studies of workers exposed to dioxin-containing products. It is generally agreed that dioxin can cause chloracne. In addition, porphyria cutanea tarda, an acquired form of porphyria characterized by chronic skin lesions and other symptoms, has been observed in some instances after dioxin exposure. Industrial workers inadvertently exposed to dioxin have complained of weight loss, easy fatigability, aching muscles, insomnia, irritability, and loss of libido but these complaints are very difficult to evaluate. Also, after such exposure, abnormal liver function tests have been reported in

association with tender liver and liver enlargement. Neurological changes in sensory function have been observed. There is evidence that there may be an association between workers exposed to dioxin-containing products and soft tissue sarcomas. This is particularly important since soft tissue sarcomas have been observed by the National Toxicology Program in mice exposed through the skin to dioxin. The human health effects of dioxin in relation to long term exposure to dioxin in either high or low dose are not known since adequate studies have not been done. In animal studies, TCDD has been shown to be a very toxic compound for many species of animals. The acute lethal dose varies widely but is as low as 0.6 micrograms per kilogram in guinea pigs. Various forms of tumors have been shown in different species, as have liver abnormalities, porphyria, abnormalities in the immune system (especially of immature animals), birth defects in mice and general toxic effects on fetuses of other species when females are fed and injected with dioxin during the period of conception. The only male animal study for birth defects was done in mice and did not demonstrate any birth defects when the male was fed, during the mating period, simulated Agent Orange contaminated with dioxin.

A great deal of research on the health effects of dioxin is underway. It is very difficult to quantify exposure in humans. The CDC Birth Defects Study may be able to determine whether there is an association between birth defects in children and service of their fathers in Vietnam where they may have been exposed to Agent Orange. The epidemiology studies of the veteran population and the soft tissue sarcoma component of that study will be used to determine whether health effects have occurred in these populations. Careful

epidemiologic studies are needed in part because of differences between the Swedish studies that report increased risks of soft tissue sarcoma and other international studies which, as conducted and reported, fail to confirm this association. CDC's NIOSH is completing a registry of workers exposed to dioxin-containing products. That registry will include 6,000 workers and will be used for information on death and its cause and on illness among those workers. The Veterans Administration is looking at the mortality among the Vietnam veterans, whether there is a difference in identical twins exposed in Vietnam, and other facets. CDC is also studying the effects on people who have been exposed to dioxin in soil in the United States. These studies are just beginning. It is difficult to predict what any of these studies will tell us.

One problem with all of the studies is that one cannot determine the actual dose of dioxin that an individual received. Therefore, misclassification of people into exposure groups could occur and lead to erroneous results. For example, it would be possible to include in a single group people who absorbed varying amounts of dioxin with people who did not absorb any dioxin. Since it would be clearly unethical to administer dioxin to humans, we may need to continue to look at animal data as a factor in making predictions about toxic effects of dioxin on humans.

There is no doubt that considerable additional research will need to be done. Some of it can be identified now. Some will become obvious as results from

studies already undertaken become available and as we have more experience with inadvertent exposures either when they occur, or at some point after a continuous exposure such as has occurred in Missouri.

I would suggest that further studies in the following areas are also needed: uptake and bioavailability of dioxin from different soils and the development of better methods for determining the amount of dioxin in the body.

Mr. Chairman, that concludes my formal remarks. My colleagues and I will be happy to answer any questions you or other members may have.

Mr. SCHEUER. Thank you very much, Dr. Houk.

I am going to ask Dr. Shepard a question. Really, it is addressed to Dr. Young.

Dr. Alvin Young recently returned from a scientific meeting in Seveso, Italy, where you were part of an investigation of the results of an explosion of a chemical plant which sent a cloud containing roughly 3 grams of dioxin over the city. You were part of a team that addressed the human health effects of that dioxin exposure.

Could you give us an update on that meeting and what your conclusions were?

Major YOUNG. I was a team of one involved in that particular review of the Italian data. A major reason for my going was to look at the issue of exposure and some of the work that the Italians have been doing on trying to quantitate exposure, the fate of the material in the environment and how this may have affected the human population.

As you may recall, the accident that took place in Seveso took place July 10, 1976, so we are about 7 years from that time period in terms of monitoring the human population.

The total amount of dioxin is about 200 grams that were disseminated on about 700 acres. Seven hundred and thirty-six people lived in that site. Of that, they estimate that well over 400 of those may have been very significantly contaminated, with about 20 percent of that total population of 700 actually developing chloracne.

One of the interesting things is it was the children who developed chloracne more prevalently. The kids the age of less than 1 year to 4 years old, 19 of them; the age from 5 to 9, 108 of them; the age of 10 to 14, 33.

There was a very clear relationship between body size and the development of chloracne, which suggested that the amount of dioxin actually was quite uniform in that area, and the amount of dioxin with regard to body size was important in the development of the actual chloracne condition.

Mr. SCHEUER. What was the percentage of kids?

Major YOUNG. Only seven adults developed the chloracne.

Mr. SCHEUER. What percentage of the kids? You gave us the number of kids who got it, but what percentage of the kids in that group or of that body size got chloracne?

Major YOUNG. Twenty percent of the entire population in terms of that size of the children. We didn't have an accurate breakout there of how many children totally. There were 187 total cases, however, of chloracne.

The monitoring effort that has gone since that time—I would just point out that although the children were exposed for about 3 weeks, there were no deaths recorded. The adults were exposed for the same amount of time, of course, but there were 3,300 deaths of animals, indicating that although the people were exposed significantly they did not die as a consequence of that exposure where animals in fact did, especially rabbits.

It is true that the folks were warned not to eat the food, the vegetables, but in fact the Italian Government has conceded that many people did continue to eat vegetables and meat from the contaminated site during those 3 weeks prior to evacuation.

In terms of the clinical findings, urinary tract infections and inflamed joint infections were found in the children, as well as the chloracne. The only thing that has really persisted over all of this time period has been the chloracne.

Studies on neurological lesions, functions of organ systems, the growth of newborn children, the rate of malformations, birth defects, the frequency of spontaneous abortions, the amount of cytological anomalies, the immunological deficiencies, frequency of infectious diseases—at this point what we can say is that there is no evidence to show that any significant amount occurred that could be related to the dioxin contamination.

There is an effort underway to establish a very thorough cancer registry. That is going to be followed for the next 20 or 30 years, at least. That may tell us something in terms of the long-term effect, but at this point the thing we know that is for sure a long-term effect is chloracne.

In the case of the children, only 5 of the 187 people that developed chloracne have shown any amount of persisting of the lesions.

Mr. SCHEUER. Chloracne was the most serious health effect that you discovered?

Major YOUNG. That is correct.

Mr. SCHEUER. Very good.

Major YOUNG. At this time. We have to note that.

Mr. SCHEUER. Dr. Houk, over the past couple of days, June 28 and 29, scientists here in Washington have been discussing the one part per billion action level in soil that was set by your centers for disease control last fall.

What conclusions, if any, did they make concerning the validity of the one part per billion action level for dioxin contamination? Is CDC considering changing the one part per billion for various conditions for sparsely populated areas, for example?

Dr. HOUK. Thank you, Mr. Scheuer.

First, I would like to correct that there is one part per billion as a national standard. It is not. We have made every effort to indicate to everybody that it is not. We have not been very successful in that effort, very obviously.

The one part per billion was established specifically around the Minker-Stout site, which is a residential site in Missouri in which children, families were living on significantly contaminated elevated standards.

There cannot be a single national standard of any magic number. It depends upon the level of dioxin, who is exposed to it, the age of the individual who is being exposed, that the population has the ability to be exposed and the pathways that may be exposed.

The one part per billion at the residential site was based upon the fact that there were children playing in the dirt and was a lifetime kind of exposure. We certainly would not be as concerned of that same level if we had an isolated, different level, higher, extremely high, if there was no chance of people being exposed, or if in an industrial plant, where you spend only 40 hours per week instead of all of the hours through the week.

On the other extreme, we would be concerned about levels down into the low parts per trillion if the dirt is being used in the food chain production, particularly the grazing of the animals, chickens

and eggs because they bioaccumulate that dioxin into the meat, it is concentrated into the eggs, and you have a very much higher level. So, in fact there is not a national standard. There can never be. There may be levels of concern in each different kind of situation in which we are now trying to do them.

As far as the group in Atlanta this week, they concluded that for residential areas the one part per billion is a reasonable level of concern.

I would like to comment, if I may——

Mr. SCHEUER. My understanding was that you were considering going to 10 parts per billion for rural areas. Not true?

Dr. HOUK. No, sir Around a specific site it may be even higher than 10 parts per billion if there is no chance of people being exposed to it.

I would like to comment on Seveso, if I can. I think it is very important, Mr. Chairman, because Seveso keeps being thrown up to negate everything of our concerns.

The explosion in Seveso, there was a cloud of dioxin-containing material put over that community. Within 2 weeks the people were evacuated, all of the vegetation was cut down and removed, and the multiple dead animals during the first 2 weeks represent, in my opinion, sir, and I think many others, acute exposure because the animals were eating the dioxin that was on the vegetation in very high concentrations.

Mr. SCHEUER. Excuse me. Were they large animals or just rabbits and small animals?

Dr. HOUK. Rabbits and small animals. There were some dogs involved, I believe.

Mr. SCHEUER. But they were sheep or cows or goats?

Dr. HOUK. Not in substantial numbers.

The important part here is we keep hearing Seveso, that nothing was found and, therefore, it negates all of our concerns for the human. In my opinion, Mr. Chairman, that is not true because that was an acute exposure to the people, who were then moved. In fact, for the chronic exposure, the people living in the area of Seveso outside of the plant now, where they lived, the level of dioxin, 0.15 is the highest part per billion, 0.15, which is very much below our level of concern in a residential situation.

Mr. SCHEUER. Thank you very much.

Congressman McGrath of New York.

Mr. MCGRATH. Thank you very much, Mr. Chairman. Dr. Houk, I was somewhat interested on page 1 of your testimony in the symptoms: weight loss, easily fatigued, aching muscles, insomnia, irritability. It sounds like my symptoms.

I am wondering what exactly are the symptoms and features of the soft tissue sarcomas?

Dr. HOUK. The soft tissue sarcoma, Mr. McGrath, is a specific form of tumor from one of the several components of the body cells. Like all tumors, it may have no symptoms. Then it may have extensive symptoms. If it is a pathologic diagnosis, it can cause death. It is a cancer, to say it in more usual language.

The remaining issue that we have to address is that since these are a diverse group of tumors, is it appropriate to lump them all

when we look at a cause from a specific kind of chemical? That answer is not out yet.

Mr. MCGRATH. In speaking of the animal test data which is available, there are certain animals that show a low tolerance to dioxin in contrast to those who show a high tolerance.

Where between these two extremes do human beings fall?

Dr. HOUK. We have no idea. We are not even helped by studies in the subhuman primate species because they, too, have varying degrees. We do not know where humans fall. Do they fall to the more sensitive? Do they fall to the more resistant? We don't know.

I believe I testified in front of this committee about 6 months ago with the idea that when we don't know, and when we look historically at toxic materials, what we know now has always been more severe than what we knew 10 years ago or what we thought we knew 10 years ago. This makes us go on a very conservative estimate of risks.

Mr. MCGRATH. I hate to get on my horse again, Mr. Chairman, but your answer to the question regarding standards, that there can be no definitive standard, once again puts me in a position of asking if there are no standards, then how can we legally prevent the production of toxic materials or nontoxic materials that have dioxin in them? How can we get into court and do this?

Dr. HOUK. The regulatory agencies can certainly make standards of what is an acceptable amount of contamination or what would be allowable in contamination of new products. What I am talking about, Mr. McGrath, is that there is no standard of what has already been applied, that is in the soil over the country as a whole, one single number to be applicable to every situation within the United States.

Each of these individuals where dioxin has been applied into soil, in the bottom of streams for bottom fish to pick up, are going to have to be evaluated individually and recommendations made specifically around that site.

Mr. MCGRATH. Dr. Shepard, in your examination of those of our veterans who served in the Vietnam war, what health outcomes have definitely been linked to dioxin exposure?

Dr. SHEPARD. Mr. McGrath, we don't have any definite health problems that we can link to exposure to the herbicides in Vietnam. I want to quickly add that we simply don't know. As I tried to indicate in my testimony, we are involved in a number of research efforts to answer that question, but as of the present time, we don't have any specific illness, even chloracne, among Vietnam veterans to be certain. There are a few suspicious cases. They are to be further evaluated, but as of the moment that is the case.

Mr. MCGRATH. Are you aware of any delayed long-term effects of exposure to dioxin?

Dr. SHEPARD. Chloracne, of course, has been alluded to, and that certainly is one. For certain in humans, I think we don't get no. There are some concerns. The whole issue of soft tissue sarcoma has been raised, and the answer to that question has not come in yet.

But in terms of other human health effects that have been certainly connected as delayed effects—I am not talking about some of the acute effects that Dr. Houk alluded to, but delayed long-term

effects—chloracne seems to be the one standout at the present time.

Mr. McGRATH. What do you know about the likelihood of our veterans in Vietnam having children with birth defects?

Dr. SHEPARD. As you know, we are involved with the CDC in a study to answer specifically that question. As I indicated, the Australians have just reported out a similar study to assess the risk of their veterans fathering children with birth defects. To date, we don't have any evidence to suggest that Vietnam veterans are having children with birth defects at a higher rate than would be expected.

I would like to point out, for the information of the committee, however, that we must bear in mind that about 4 to 5 percent of all live births will have some form of birth defects, so the tragic development of a birth defect is not a very unusual event. When we are talking about a population of some 2.5 million veterans, we will have to expect some of those, unfortunately, to father children with birth defects.

It is a grave concern, obviously, and it is a tragic event when it does occur. But I think we have not yet been able to link that event to exposure to herbicides in Vietnam.

Mr. McGRATH. How long would it take statistically, how many instances over how many generations, to prove that there is a link between exposure to agent orange and dioxin and either birth defects, deaths, or some carcinogen?

Dr. SHEPARD. I am not a geneticist, but I think it is accurate to say that we will have reasonably good evidence when these studies are completed. That will be relatively soon.

In terms of the possible long-term—that is, several generations—outcome, of course, it would take, if one were to use the epidemiological approach, a study of those events to occur. However, I think that it is unlikely that there will be such an outcome over a period of time.

I might differ, if I may, to Dr. Moore, who has been very interested in this subject and has done a lot of research in animals. You might want to pose that question to him.

Mr. McGRATH. Dr. Moore, would you care to tackle that one?

Dr. MOORE. There was a study conducted, because of the alleged concerns and fears of Vietnam veterans that they may be siring children with an increased instance of malformation as a consequence of having served in Vietnam, in which mice, which have been shown to be a sensitive species to dioxin exposure, were fed simulated agent orange, if you will, at doses that were maximum that they could tolerate without becoming overtly sick. They, in turn, were mated to females.

There was no evidence whatsoever of either a decrease in fertility of those males, an increase in miscarriages or resorptions on the part of the females that became pregnant by these males, or an increased incidence of birth defects in the offspring, suggesting that when you put that together with the fact that there is very little evidence to support that dioxin may affect its toxic potential to normal genetic damage, the two together suggest that is not one of the major concerns.

Mr. McGRATH. Thank you.

Mr. Chairman, I have no further questions.

Mr. SCHEUER. Congressman Harkin?

Mr. HARKIN. Thank you, Mr. Chairman.

Dr. Shepard, are you aware of the study done in England by Dr. Ward?

Dr. SHEPARD. Yes, sir, I am.

Mr. HARKIN. Have you looked at that study? Has it been examined by the VA?

Dr. SHEPARD. Yes, sir.

Mr. HARKIN. You don't even refer to it in your testimony at all. I am concerned. Is there any validity to it at all?

Dr. SHEPARD. Maybe I could just set that into the context of my understanding.

It was not truly a study in the usual sense of the word. Dr. Ward performed for Dr. May, who was doing an analysis of the health outcomes of workers exposed to dioxin as a result of a plant accident in Devonshire, England in 1968.

Dr. Ward did an analysis of immune globulins in a group of individuals who were exposed. It is my understanding that that showed that there were some minor alterations in some of the immune globulins of the exposed group.

Those results were not deemed to be, at the time, apparently, in England, sufficiently significant to be included in Dr. May's ultimate report. Furthermore, a United Kingdom Advisory Committee on Pesticides did review those data and deemed that they were not considered to be clinically significant. In addition, the people in whom these minor aberrations did occur were deemed not to have had any significant health changes as a result of these alterations.

That is my understanding of the situation, sir.

Mr. HARKIN. I see. Does the examination he performed lend itself to further studies along this long-term breakdown of the immunological system in humans due to dioxin exposure?

Dr. SHEPARD. Yes, sir. Clearly I think we need to know an awful lot more about the effects of dioxin on the immune systems of animal species and humans. I think this is one of the areas that needs more study.

Mr. HARKIN. It seems to me, whether we are looking at the Seveso thing or Times Beach, we are looking at very near-term phenomenon that has happened to people, as you pointed out, Dr. Houk.

The veterans who I come into contact with are people who were exposed to dioxin 13 to 15 years ago. In many cases some valid reports that I have had confirm birth defects in children occurring 10, 12, or 13 years later in individuals who were exposed to dioxin in Vietnam.

I am wondering if perhaps we aren't narrowing our focus a little bit too much on the short term and not looking at the long-term effect, which might lend itself to this kind of thing, this breakdown—I am not a doctor, obviously, and I don't pretend to know about it—in the immunological system of humans that may make them more susceptible to other things.

Dr. SHEPARD. Certainly those questions are involved in a number of research efforts that are now ongoing and which will be in individuals who have had their exposure at some time in the past.

Mr. HARKIN. Let me ask you this. When a veteran comes in and complains that he has been exposed to dioxin, there are certain things under a certain law that we passed here a couple of years ago that VA has to do, to examine him for certain things.

Do you examine, do you do any kind of study on that person's immunological system at all? Is there anything like that that is done?

Dr. SHEPARD. That is not one of the prescribed tests to be done in those individuals who come in for the so-called agent orange examination, which is a registry of Vietnam veterans, of whom we have now examined some 118,000.

That is not one of the routine tests that is prescribed. However, if there is any condition which is observed in any of these veterans, it certainly would be and I am sure has been an appropriate study to do as part of a general workup of that individual's particular problem. But it is not a routine study.

Mr. HARKIN. Let me follow up. The VA has been aware of the Ward study, as I understand it, since at least 1980 or 1981. I know EPA has been aware of it since 1980. When did the VA first become aware of it?

Dr. SHEPARD. I think we actually heard about it quite recently because that report was a confidential report to Dr. May. It was never published in the scientific literature and to my knowledge has still never been published in the scientific literature. So, it would not have come to our attention in the usual course of events. However, because of the recent concern, it has.

Mr. HARKIN. What I am getting at is this. My primary concern here with the veterans is that numerous veterans—in fact, I just met with some over the weekend. One of them told me that when he went in for his agent orange—he had been in that area in Vietnam and knew that he had been in the defoliant area. He went in, and the only thing they checked him for was chloracne. That was it.

I see you shaking your head, Dr. Young.

Dr. SHEPARD. If I may, sir, I think it is unlikely that was the case. For him only to have been examined for chloracne—I wasn't there, obviously I can't say from personal observation———

Mr. HARKIN. I can't say either. I only know what he told me.

Dr. SHEPARD. I think it unlikely that a Vietnam veteran going in for an agent orange examination would only have been examined for chloracne.

Mr. HARKIN. Well, again, as a followup, based on the Ward results of a few individuals that he checked over a long period of time, is the VA looking at implementing a new testing procedure to test these veterans along these lines? If not, why not?

Dr. SHEPARD. We haven't implement such a study because the information that we have to date suggests—from the Ward study and from Dr. Ward himself, as reported in various areas—that he did not consider his results to be of clinical significance.

Mr. HARKIN. That sounds like a term of art to me. What does clinical significance mean?

Dr. SHEPARD. That is that the alterations that were detected by Dr. Ward were not of sufficient magnitude to suggest that that

person was or people were subject to significant health problems. This is——

Mr. HARKIN. Wait a minute. Were not subject to significant health problems. Now we are getting into other terms of art. Did not the Ward study conclude—I don't know if I can say conclude, but did he not draw a direct linkage between exposure to dioxin and breakdown in the immunological system of those individuals?

Dr. SHEPARD. No, sir. There is a difference between a breakdown of the immunological system of those individuals and some laboratory differences in a couple of the immune active chemicals of the body.

What I am trying to point out is that those changes that were a laboratory detection were viewed as not having a serious potential for causing disease or leading to disease or contributing or making individuals more susceptible to serious illnesses.

I think it is a very interesting research question and one that should be pursued. I think because of this lack of evidence that it has, in fact, contributed to significant illnesses that we have not embraced it as one of our routine laboratory studies.

Mr. HARKIN. Why not? Why not do it? Does it cost a lot of money? Why couldn't you do it as a routine study?

Dr. SHEPARD. We could do it. We could do it as a routine. As I say, the reason we haven't is that we have not viewed it as a clinically important problem.

Mr. HARKIN. I think I am beginning to understand that. But it would seem to me that there is at least some indication of connection there.

Dr. SHEPARD. Another point that I should have made is we are looking at some of the other studies, particularly the Air Force Ranch Hand study. We haven't talked a lot about that this morning. That, of course, is a very significant epidemiological study which will be reported out very soon.

Mr. HARKIN. These are the pilots, right, and the air crewmen?

Dr. SHEPARD. Well, all the crew members involved in the spraying missions compared to very closely matched controls. That is a part of the Ranch Hand study. So, before we embark on an additional piece of research, we have been awaiting the results of the Ranch Hand study. They did do some of these immunological assays among the pilots. If that study suggests that there is a significant alteration, then certainly we will look at the appropriateness of——

Mr. HARKIN. I have some real concerns about the Ranch Hand study in terms of how they were exposed and how the ground troops were exposed in terms of ingestion of water, the direct contact with the foliage.

I remember one Vietnam veteran telling me that he used to walk through these areas after they had sprayed. The stuff would get on their skin, they would sweat, they would wipe their face, it would get in their mouth, get in their eyes.

I am wondering if really there is that much of a connection between those air crewmen and the pilots who flew the planes and those individuals who were on the ground, who had that stuff sprayed on them.

Dr. SHEPARD. I don't think there is any question, sir, that the members of the Air Force Ranch Hand crew were heavily exposed, and exposed day after day. Their exposure obviously was different, but I don't think it is any evidence to suggest that it was any less.

Mr. HARKIN. Thank you, Mr. Chairman.

Mr. SCHEUER. Thank you.

We have a rollcall vote well on its way, so we are going to suspend for 10 minutes. Then we will be back to complete the questioning. We apologize for the interruption.

[Recess.]

Mr. SCHEUER. The subcommittee will come to order.

Congressman Volkmer.

Mr. VOLKMER. Thank you, Mr. Chairman. I do wish to thank you specifically for the opportunity to ask some questions, even though I am not a member of the subcommittee, and to stand in. Being from the State of Missouri and having a few sites contaminated with dioxin, I do have some things of concern to me.

Dr. Houk, I am sorry I wasn't here for all of it, but I had another subcommittee meeting. As I came in, I thought I understood you to say to the effect that the criteria of one part per billion is not necessarily a criteria, really. Is that what you said?

Dr. HOUK. It is a level of concern, Mr. Volkmer, that was designed specifically around the Minker-Stout site, a residential site with families growing up, children playing in the dirt, and a lifetime of exposure.

Mr. VOLKMER. That would apply also to the Quail Run site, which is in my district, which has the housetrailers?

Dr. HOUK. Yes, sir. It would also apply to Times Beach.

Mr. VOLKMER. It would apply to such places, which has really been abandoned now, which is the first site ever found, I believe, Shenandoah Stables, which was used by humans, of course, along with animals?

Dr. HOUK. Yes. I believe Shenandoah is cleaned up to significantly below that level.

Mr. VOLKMER. I mean if it was, let's say, to the same level?

Dr. HOUK. Yes. Shenandoah Stables would be different than a residential site, if you are talking specifically about the stable, because the riding of the horses, the kicking up of dust, et cetera, would have a different pattern of exposure as opposed to children playing in the dirt in their yard.

Mr. VOLKMER. You are conducting health studies on people from Times Beach and Minker-Stout, et cetera, are you not?

Dr. HOUK. Yes, sir, we are.

Mr. VOLKMER. How long will those continue?

Dr. HOUK. The initial phase will be an analysis of what has been done so far. Sometime, Mr. Volkmer, within the next 2 or 3 months, we will take a look at that data and decide two things: what additional things need to be done or additional populations around those sites need to be included in those studies.

We have the individuals that we have contacted into a registry of people, which we will keep active followup indefinitely, at least for 10 years, and probably more than that, for three purposes: one, to see if there are other long-term health effects; that if some medical breakthrough occurs, if we can measure dioxin and their values or

if there is some treatment available, we can contact those people and apprise them of this; and the third reason is if they have surgery for any other reason, to enlist the help and their surgeon to collect a specimen of fat that can be stored until such time as we have the technology to do dioxin levels in fat tissue, so that we can go back and retrospectively get an idea of what the exposure of each individual was and then further re-analyze the study and hopefully provide some more concrete, less nebulous answers.

Mr. VOLKMER. So this will be an ongoing thing and could even go past the 10 years?

Dr. HOUK. Yes.

Mr. VOLKMER. To get back briefly to the one part per billion and the controversy, you say an area of concern—I can't think of the person's name at Washington University who started the thing with the American Medical Association—what do we mean by "area of concern?"

Dr. HOUK. We would think that people from children on up should not be exposed to anything higher than this level for the remainder of their lifetime. At Minker-Stout we made the recommendation to the Environmental Protection Agency that people be prohibited, prevented is a better word than prohibited, from being exposed at this level; that somehow there be a barrier put between people and that soil.

Mr. VOLKMER. Dr. Kimbrough, do you have any comments you wish to make in regard to the area I just covered?

Dr. KIMBROUGH. I guess I would like to add that one would not have to be concerned if one were exposed to such concentrations for a very short period of time. What we are primarily concerned about is that people are exposed to these levels over many years, and that that needs to be prevented.

Mr. VOLKMER. Mr. Young, in your opinion, do you feel that dioxin as we know it, TCDD, is harmful to humans?

Major YOUNG. I think it definitely is. I think the data shows that certainly dioxin is harmful to humans. What we don't know and what we are trying to find out is what the long-term consequences of that exposure might be.

Mr. VOLKMER. We don't know that it isn't, though, either, do we?

Major YOUNG. We don't know that it isn't?

Mr. VOLKMER. That it is not harmful to humans.

Major YOUNG. Oh, no, we don't know that it is not.

Mr. VOLKMER. In other words, over the long run we don't know that it does not have adverse effects or whether it is carcinogenic or what type of harmful effect it has on humans?

Major YOUNG. We may not find that there is any long-term, 20- or 30-year consequence outside of chloracne, but we may. The data are not all in. I think that is the important thing to remember.

Mr. VOLKMER. So, we do not know yet what the long-term effect is on our veterans who served in Vietnam, who were exposed for a period of time to agent orange or other dioxin-contaminated materials, do we?

Major YOUNG. I think we will begin to get some feel for this when the Air Force Ranch Hand study is released within the next few months.

Mr. VOLKMER. Thank you, Mr. Chairman.

Mr. SCHEUER. Thank you.

Congressman Ridge of Pennsylvania.

Mr. RIDGE. Thank you, again, Mr. Chairman, for the courtesy. It is sincerely appreciated.

Mr. SCHEUER. We are delighted to have you with us today.

Mr. RIDGE. It is a matter of personal interest that we don't discuss on the Banking Committee, for obvious reasons.

Mr. SCHEUER. You have a great deal to contribute to this particular set of hearings tnat is not duplicated in the knowledge or the experience of any other member of this committee on either side of the aisle. We are absolutely delighted to welcome you here.

Mr. RIDGE. Thank you, Mr. Chairman.

Dr. Shepard, you referred to a variety of studies. One involves 500 twins, one sibling in Vietnam, one stateside or elsewhere, Australian troops, and a study of men now deceased after their Vietnam tour.

Are all 500 twins, are all the Australian troops and are all the deaths that you are studying of men who were exposed to agent orange?

Dr. SHEPARD. We don't know that yet until we identify the individuals. Let me, if I may, point out some particulars of those studies.

The identical twin study will be of Vietnam veterans. We have yet to identify those twins. We are in the process of setting up a registry of identical twins, one of whom served in Vietnam and one of whom was in the military but did not go to Vietnam.

We won't know until we have those twins identified as to whether or not they were exposed to agent orange. The principal focus of this study is not to determine the effects of exposure to agent orange but rather to determine the effects of service in Vietnam.

Now, it is possible that if we come up with say 200 or 300 twins in whom we can establish that they were, in fact, exposed, then we will possibly be able to draw some conclusions in that regard. But it is not the principal focus of that study to do that.

Mr. RIDGE. Was it the principal focus of the study involving the Australian troops to do that?

Dr. SHEPARD. You mean the birth defects study?

Mr. RIDGE. Correct.

Dr. SHEPARD. No. In their report they were not able to muster the records necessary to determine which of their troops were exposed and which were not.

Mr. RIDGE. I presume that the study of the deaths subsequent to service in Vietnam would not have that focus, either?

Dr. SHEPARD. I think there is a greater opportunity that that will be the case. We have identified the 60,000. We are now in the process of looking at their military records to establish whether or not they served in Vietnam.

Having done that, there will be an opportunity to identify—and in that process we are identifying the military units with whom they served—and we will then have an opportunity to go back into the operational records to determine which of those individuals who served in Vietnam had a high likelihood of being exposed.

In that group there may well be the opportunity to look at death patterns between individuals who were likely to have been exposed and those who were not likely to have been exposed.

Mr. RIDGE. I guess my concern is that there is, again, a public perception that these kinds of studies and the conclusions that have been drawn and testified to at this hearing, that some of them indicate that there are no long-term effects resulting from exposure to dioxin.

The twin study, it is not targeted to veterans who were in Vietnam who were exposed to dioxin. If they happen to have been targeted, that will be part of the study. The Australian troops did not involve an inclusion of only those who had been exposed. Neither did the 60,000 deaths that you are going to consider.

My question I guess basically to the entire panel is would not this limited—and I realize that your scientific interests have greater implications, industrywide implications, international implications, but I am coming from a very personal perspective and you are talking about millions of veterans who served.

Dr. SHEPARD. The major epidemiological study which is now being undertaken by CDC will answer that precise question. It is designed to answer that precise question.

I would defer further to Dr. Houk, but the study is divided into two main portions: Those cohorts who had a likelihood of exposure or who are documented to have had a high likelihood of exposure, and compare them to troops who served in Vietnam but had little or no likelihood of exposure.

The epidemiological study mandated by Congress will be answering that question.

Mr. RIDGE. Will you tell me a little bit more about that, Dr. Young, that study?

Major YOUNG. Dr. Houk is the most appropriate to talk about that CDC study.

Mr. RIDGE. Doctor, would you kindly enlighten me?

Dr. HOUK. The CDC study, which is out for review at OTA and other various groups at the moment, has three basic purposes: to look at exposure to agent orange; Vietnam veterans in the area of Vietnam where it was used under similar combat conditions, who were very likely exposed; and a group who were likely unexposed. We are reasonably certain that we can develop these records through the Army Agent Orange Task Force under Mr. Dick Christian's very able leadership.

Each of these cohorts, Mr. Congressman, will have 6,000 individuals. We will take another 6,000——

Mr. RIDGE. I am sorry, what was the sample size?

Dr. HOUK. Six thousand in each of the cohorts I will describe.

Another group will be of combat veterans in Vietnam in an area where no herbicides whatever were used, recognizing that the combat situations and the other things are different, but that may help reinforce some of the differences or unreinforce some of them, if any are found.

In addition to that, we are taking a group of 6,000 cohorts each, a Vietnam experience study, a random sample of people who served in Vietnam during specific years and people who did not serve in Vietnam but were from the same MOS's, the same category, where

we were reasonably certain that whether you were sent to Vietnam or did not go to Vietnam was really a flip of the coin, not different MOS's, that you would wind up in Germany as opposed to someplace else.

The third and a very critical component of that study is going to be looking at the soft tissue sarcoma issue, to do a case controlled study using the seers centers, which is the end result of cancer registries. I have forgotten precisely the States and the cities that they are located in, but it comprises 25 million people, 10 percent of the population.

There is no evidence that those populations served in Vietnam any differently than the ones who are not included. The ascertainment of tumors in there is virtually 100 percent complete, so that is an entire population study that will be looking at that very important issue.

The CDC birth defect study, also in answer to Mr. McGrath's question, was designed and is being executed. We think that we know that it will be executed in a way that if there is a 20-percent increase in birth defects we will be able to detect that with 70-percent assurance. If there is a 50-percent increase, we will be able to detect that with over 95-percent assurance. That is for service in Vietnam.

Each of the individuals who served in Vietnam and who were Army veterans, we will go back, again, through the Army agent orange task force, and search their records out, to try to determine as best we can whether or not and how much exposure—principally whether or not they would have been likely to have been exposed to agent orange in Vietnam or they were likely not to have been exposed to agent orange in Vietnam.

The other issue that frequently gets involved is the issue of women in Vietnam. We are actively engaged, again, with the Army agent orange task force, looking at a sample of 1,000 names that we have, to see that we will be able to find any of the women because of name changes, the absence of social security numbers and stuff. If you can't find them, it doesn't make sense to mount a very expensive study that is going to have inconclusive results or negative results.

We would like also to point out, as it relates to the Vietnam veterans and to Mr. Harkin's concern about the long-term exposure, people in Times Beach, the dioxin was sprayed in the Missouri areas in 1971 and 1972. That is 10 or 12 years of exposure to that already.

A member of my staff was in London 2 weeks ago and met with Dr. Ward and discussed the immunologic problems with Dr. Ward. His recommendations to us were no different than we had received from our consulting with other immunologists in this country about what we should look for both in the Vietnam part of our studies for the veterans and the immunologic process and that we have already included into the study of the populations of the United States.

Mr. RIDGE. I appreciate that extensive reply. It generally does answer a concern that I have. I guess I was just curious.

It is probably a question of methodology—and I leave it to the scientific community as to how they go about it—but clearly there

are men who can be identified who were exposed: The men who took it out of the barrels, dealing with it day to day, the defoliant, the combat soldiers who were underneath it when it was either sprayed or during the monsoon season when it came down, as one Congressman testified, walking through the jungle and it was falling off the leaves and the perspiration.

These people can be identified. Yet, until the CDC study—and even now we are talking about we are going to have some twins, some maybe have been exposed, and instead of identifying the people who have been exposed at the end, it seems as if the methodology says we will run our tests and after they are concluded we will go back down and see how many were exposed. At least part of this program that you are running is going to identify these people up front for testing and evaluation purposes.

Dr. HOUK. Yes, but we cannot, Mr. Congressman, allow people to identify themselves to us. That self-selection would put so much bias in the study that it would be unacceptable in a scientific framework.

The thing is that we are identifying units that have certain characteristics of exposure, down to the company platoon unit, within half a kilometer or so many kilometers of a Ranch Hand spray mission within 3 days or 7 days, who were associated with the helicopter spraying, associated with base perimeter spraying, associated with several different kinds of characteristics, to an exposed group who have none of those characteristics, and to an unexposed group who served in the same area at the same time in Vietnam.

We will physically identify each of those individuals who served in those units and then set out on a very extensive tracking procedure, to get as many of those as we can, and get them involved in the study. Our estimate now is we have to have somewhere in the neighborhood of 70 percent.

As you are well aware, this is going to be a big job doing that. We invoke the help of the veterans' organizations and everybody else that we can, once we have identified the name, social security number of a person, to try to find that individual 10 years or 15 years later, to invite him to participate in the study.

I think the experience that we have from Ranch Hand, the experience that we have from the CDC birth defects is that once we have identified that veteran there is no reluctance to participate, or there is very little reluctance. They will participate. The problem is identifying the individual.

Mr. RIDGE. I appreciate that, Dr. Houk. I can well understand why the self-identification process is not something that you want to undertake. I think you are going about it the right way.

Can you give me an idea as to the length of time you feel you need to identify these potential participants, the kind of studies you are going to be conducting and when the Vietnam community and the public in general might be aware of your findings?

Dr. HOUK. The identification of the cohorts has already proceeded by the Army.

Mr. RIDGE. By the Army?

Dr. HOUK. By the Army agent orange task force, which is using that for this, in a Herculean effort which is being superbly done.

As soon as our protocol is reviewed and out, we will do death record searches of the country to make sure that the individual has not died, that the individual is still alive. Those who are dead, we will do mortality studies. The ones who are alive will have a very extensive physical and laboratory examination for a portion of each of those cohorts. Each of them will have a very extensive questionnaire.

The Vietnam study, the agent orange study, are similar but quite different in some of the outcomes. We are looking at as broad a spectrum of outcomes as we can that has been suggested by the animal research literature.

The study will be reported in various components. We anticipate that it will be completed by September of 1987. The OTA has reviewed this and suggested that this is a very optimistic timeframe. We agree that it is optimistic, but we will do our best to try to comply with it.

Mr. RIDGE. Mr. Chairman, I want to thank you for the courtesy, again, and would ask not as a matter of the record, but the indulgence of the panel, if I might follow up with some written questions.

Mr. SCHEUER. There being no objection, so ordered. That would be true for any member of the panel.

Let me ask you, before we suspend for this next rollcall, do any of you have any questions or any comments you would like to make concerning any testimony or any of the comments your colleagues at the witness table have made this morning?

Then I am going to ask you if any of you would like to react to the piece of paper that you have heard about that has been issued by the AMA, both the "Whereas," clauses and the "Therefore," clauses, either one?

Dr. Shepard?

Dr. SHEPARD. Thank you, Mr. Chairman.

I would like to follow up on a comment that Dr. Houk made earlier. I think he was asked where do humans fall in the scale of toxicity, the range of toxicity. I think I heard him say that we have no idea.

If I am misquoting him, I apologize, but I don't think that is entirely accurate. We have some ideas based on what we have seen of the Seveso experience—granted, that was an acute exposure, but I don't think that negates the evidence—what we know of humans who have developed chloracne as a result of exposure to dioxin, clearly evidence that they were exposed, and a long-term followup of those individuals.

I think we do have evidence of where humans fall in this scale. As I say, if I am misquoting Dr. Houk I apologize, but I think I need to say that for the record.

Dr. HOUK. I don't think you misquoted me, Barclay, but obviously your philosophy of making bets is different than my philosophy of making bets.

Mr. SCHEUER. That is what makes for horse races, Dr. Houk.

Dr. Kimbrough.

Dr. KIMBROUGH. I would like to add something. When I looked through the literature to determine what we could use for our risk assessments when we had to give guidelines for levels of dioxin in

soil, I was unable to find any doses in the literature that were related to human exposure.

All of the experience that we have with human exposure is very qualitative. So, at the moment we really can't say where the people are, whether they are less sensitive than the guinea pig or similar to the hamster or whether they are more like subhuman primates. We just don't have any idea.

Mr. SCHEUER. Are there any other comments? Well, we thank you very much. The hour is late. We appreciate your attendance. It has been an extremely interesting hearing.

Indeed, because the hour is so late and because most of our members on both sides of the aisle have had to pursue other concerns of theirs and other responsibilities, we are going to postpone the second panel this morning until after the recess, which is going to start about 3 this afternoon for us. We will schedule that second panel, with apologies to them, sometime right after July 12. We hope we will see you all back again.

Thank you all very much. The hearing is adjourned.

[Whereupon, at 1 p.m., the subcommittee adjourned.]

DIOXIN—THE IMPACT ON HUMAN HEALTH

WEDNESDAY, JULY 13, 1983

HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE AND TECHNOLOGY,
SUBCOMMITTEE ON NATURAL RESOURCES,
AGRICULTURE RESEARCH AND ENVIRONMENT,
Washington, D.C.

The subcommittee met, pursuant to notice, at 2:11 p.m., in room 2318, Rayburn House Office Building, Hon. James H. Scheuer (chairman of the subcommittee) presiding.

Present: Representatives Scheuer, Mackay, Volkmer, McGrath, and Schneider.

Staff present: Anthony Clark, Mary Beth McJury, Charles King, and Charles Cantus.

Mr. SCHEUER. The subcommittee will come to order.

Unfortunately it looks as if we are going to have a vote in another 10 or 15 minutes according to Congressman McGrath.

There is a further misfortune, our computer voting system seems to be on the fritz. So we can't have a quick 10- or 12- minute recess. They have to read through all the names and that takes an eternity.

To go through it twice takes about half an hour. But what we will do is, in order for Congressman McGrath and I to make it on the first time around, we'll recess immediately, OK, Ray, when the bells go off.

We'll get over there by the time they come to the M's, and then you can come back and I'll be back by the time they get to the S's.

Why don't we get started. OK. We'll probably have a 15- or a 20-minute recess at that time. We simply beg your indulgence and apologize.

Today I would ask unanimous consent for both Congressman McGrath and me to make statements for the record. We had a day of hearings. Nothing has changed very much as to the purpose of these hearings.

What we are in effect trying to do is to find out how much we know about dioxin, what the health impacts are, the health threats are to human beings. Considering the research base and the knowledge that we have now, what further information and what further analysis and what further knowledge do we have to accrue in order to come to some reasonable conclusions as to what tolerable levels of dioxin would be.

We want to take this whole matter out of the arena of emotionalism and hyperbolae in which it too often has been found. Is that fair enough?

Having said that, both of our full statements will be placed in the record at this point.

[Opening statements of Mr. Scheuer and Mr. McGrath follow:]

OPENING STATEMENT ON DIOXIN HEALTH EFFECTS BY HON. JAMES H. SCHEUER, JULY 13, 1983

The Subcommittee will come to order. Today, the Subcommittee continues its hearings on dioxin and its potential public health problems.

At our first hearing on this matter on June 30, we heard testimony that dioxin may well pose some serious short-term and long-term adverse health effects.

Indeed, at that hearing the American Medical Association rescinded the implication of its previous statements that dioxin does not pose a serious public health problem.

It is clear to me from this clarification by the AMA and from testimony presented by other witnesses that dioxin is truly a serious matter which must not be dismissed as hysteria.

While it is true that many unanswered questions remain about what dioxin may do to people, I do not believe this is sufficient reason to dismiss the problem as insignificant and to council against remedial action. To do so would be irresponsible.

The available evidence on dioxin health effects is substantial and the focus of the hearing today is on how this evidence is being interpreted. Specifically, we will examine the use of dioxin health effects data in establishing what dioxin concentration levels, if any, constitute a health hazard to man.

Assisting us in this task are representatives of the Food and Drug Administration and the Environmental Protection Agency. Gentlemen, thank you for being here and please accept my apologies for the inconvenience we may have caused you.

Before we proceed, I would like to turn to the Ranking Minority Member of the Subcommittee, Congressman Ray McGrath, for any opening remarks he may wish to make.

HON. RAYMOND J. MCGRATH, HEARING ON DIOXIN—THE IMPACT ON HUMAN HEALTH, JULY 13, 1983

Thank you, Mr. Chairman. I want to join you in welcoming our witnesses here today, and state that we really appreciate them coming before us again.

The amount of interest shown by our members in this issue at our last hearing indicates that we are all quite concerned about this possible environmental threat.

I think our witnesses today will be able to provide us with valuable information regarding dioxin contamination in our food supply and also how we are attempting to deal with dioxin in our environment.

I look forward to their testimony.

Mr. SCHEUER. We will now call on our two witnesses.

The witnesses will have their prepared statements printed in full at this point in the record. Perhaps you could chat for 8 or 10 minutes, more informally, summing up your testimony. You can come one after the other. Then I am sure we will have questions for you.

The first witness will be Dr. Sanford Miller, Director, Bureau of Foods, Food and Drug Administration.

Dr. Miller, would you like to come forward at this time?

STATEMENT OF DR. SANFORD A. MILLER, DIRECTOR, BUREAU OF FOODS, FOOD AND DRUG ADMINISTRATION, PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES, ACCOMPANIED BY DR. W. GARY FLAMM, ASSOCIATE DIRECTOR, TOXICOLOGICAL SCIENCES, BUREAU OF FOODS, FOOD AND DRUG ADMINISTRATION

Dr. MILLER. I thank you, Mr. Chairman.

We appreciate the opportunity to testify on the human health effects of 2,3,7,8-tetrachlorodibenzodioxin [TCDD].

With me today, as you pointed out, is Dr. Gary Flamm, who is Associate Director, Toxicological Sciences, Bureau of Foods, Food and Drug Administration. He will also be available to enter into the discussion.

Mr. SCHEUER. That is excellent. We are delighted to have you, Dr. Flamm.

Dr. MILLER. I will not discuss in any great detail our responsibility and jurisdiction over food committees. I am certain that the committee understands what those are.

What I would like to do is give primary emphasis to the issues you raised in your letter of invitation, and give attention to some of the issues which were addressed in the prior day of testimony.

As you already heard from scientists at the National Institute of Environmental Health Sciences and the Centers for Disease Control, TCDD is an extremely toxic compound causing a variety of toxic effects. Included among these are birth defects, cancer, immunotoxicity, and so on.

As you also know, most of what we know about TCDD is derived from animal studies, particularly studies in rats and mice, and to a lesser extent, in guinea pigs.

Unfortunately, as you also heard, based on our present knowledge, we can't reliably state whether or not humans are more or less sensitive than the animal models that have been used to explore the toxicity of TCDD.

Nevertheless, in recommending the concern levels for TCDD that we did in Great Lakes fish, at 25 and 50 parts per trillion, we in fact acknowledged extremely potent toxicity of TCDD as determined experimentally using those animal models.

I just would like to point out to you that the substance which we had believed in the past to be one of the most potent carcinogenic substances found in this food supply, aflatoxin, the action that we established for that was a thousand times higher than the one we established for TCDD. This, I think, reflects the concern that we have over TCDD.

It is important to recognize that in establishing either a tolerance or an action level, or in fact recommending a level of concern, FDA is both guided and constrained by statutory authority. Even the statutory authority might not apply to a particular situation, the Agency still operates as it did. It's part of the operational milieu of the Agency, if you will.

Thus, if the substance in question is unavoidable by good manufacturing practice, we have to establish a level which protects the public health, while at the same time avoids a needless reduction in the food supply. This is a very important component of the decision process.

We must maintain the availability of food while at the same time protecting the public health. This, I am sure, as you realize, is often a very difficult decision.

Although there are many who would argue that the data available now on TCDD is not sufficient, in our opinion it is sufficient to establish what we consider to be a worse-case risk estimate in order for us to do our regulation.

Based on this evaluation of the data, we stated in our advisory that fish containing 50 parts per trillion should not be consumed,

while fish containing more than 25 but less than 50 parts per trillion should not be consumed more than twice a month.

We further stated that based on this kind of evaluation, we did not believe that there was any general public health problem at levels below 25 parts per trillion in the areas we believed were affected along the Great Lakes. That's a very important point.

Again, I want to emphasize that these are not tolerances. They are action levels. These are different kinds of regulatory actions. But instead, they are what we call levels of concern in which we provide advice, which I have been asked for by several of the Great Lake States.

Since those Great Lakes are shared by Canada, we attempted to harmonize those levels with those of the Canadian Health Protection Branch. We have continued to consult with those colleagues in Canada and in the United Kingdom and in the EPA for that matter on this issue. In fact, we are going to meet with them again in September to discuss the issue more fully.

There are several reasons, which if you like we can discuss later on, as to why we did not formally prepare and defend an action level or a tolerance for TCDD throughout the country as a whole. Just to make one point, such a formal action on our part would be very slow and laborious in our process, and certainly challengeable in the courts.

At that time we would have to defend the proposition that the fish so contaminated in any of these levels would be contaminated by a poisonous and deleterious substance which may have rendered the fish harmful to human health everywhere under ordinary conditions of use. This is a very difficult thing to do.

The concern level which we did set was, as I said, designed to provide guidance to individual States that were confronted by the problem, and to reflect that we believe the apparently restricted nature of the food contamination problem since we did not have any evidence then, nor do we have now that TCDD contaminated food is in the food supply in general.

Mr. SCHEUER. I did not get that.

Dr. MILLER. I said, sir, that we established this as a concern level because we were convinced that this was, based on the data we had then, and indeed the data we have now, that food contamination problems were restricted to those areas in the Great Lakes that had been contaminated by the outflux of these plants, and second in those other areas in the country where plants had in fact released TCDD-containing material into the food supply.

There was no general contamination of food throughout the United States with TCDD.

Mr. SCHEUER. Yes.

Dr. MILLER. As I said before, that this level was established only for the specific situation of the fish in the Great Lakes. I keep emphasizing that because this is really an important point. It is impossible to set one uniformly for everywhere, which is part of the problem.

We arrived at this level of 25 parts per trillion, which is of course the actual level of concern, in the following way. We looked at the distribution of TCDD in fish in the affected area. From that

we determined the fact that it was mostly carp and catfish that were contaminated—bottom-feeding fish of one kind or another.

Keeping in mind our statutory requirement to consider both public health and availability of food, we evaluated several possible levels of concern ranging from 10 to 1 hundred parts per trillion. We determined, based on that, that the 25 parts per trillion represented the level of risk acceptable to public health while resulting in a minimal impact on availability of Great Lakes fish as a food source.

Without going through the details of this, let it suffice to say that using the data which we had from food consumption surveys, in which we could determine the 90th percentile of fish consumption in the Great Lakes, and looking at the pattern of consumption of fish from those areas, we came to the conclusion that an individual at the 90th percentile of consumption, would consume, making all the most conservative estimates, eating only catfish and carp, all from the most highly infected areas, would have a daily exposure to TCDD of around 392 picograms per day.

The fact of the matter is that at that 25 part per trillion level if we want to assure ourselves as we do that the 25 part per trillion residue level is not being exceeded, that actual average intake would be about one-third of that. It would be somewhere in the order of magnitude of 8 to 10 parts per trillion.

This then actually reduces the actual exposure level to somewhere in the order of magnitude of about 130 picograms per day. It is interesting to point out that that 130 picograms per day is about the same as the lower level estimated by CDC based on their one part per billion level which they established for the soil in Missouri.

We can further adjustments in this. I mean it's unlikely that anybody is ever going to consume fish only from the contaminated areas, and that only bottom-feeding fish would be consumed, et cetera. If you make all of these adjustments to this, and I think they are reasonable adjustments, we come to the conclusion that the actual intake is in the order of magnitude of 13 picograms per day. These are people at the highest level of intake.

We estimate a risk to this based on several of the animal studies. This comes out to be a risk in the order of magnitude of 3 in 10 to the minus 6 lifetime risks. The possibility upper limit of 3 excess cancers in 1 million.

On a yearly basis this reduces even further. It is maybe 4 in 100 million. The risk is relatively small. The statistical risk is very small. These are not actuarial risks. In fact, it is likely that we have way over estimated the risks. These are statistical approximations of what we can expect. They are done largely for the purposes or regulation to give us some idea of the relative importance of this as a toxic material.

In addition, that 25 parts per trillion also represents about what we consider to be the limits that we set given the current state of the art and medical technology. If we go any lower than that it would push the technology beyond where we could deal with it.

Current technology can detect 10 parts per trillion. We feel that is exactly the level required in order to insure that 25 parts per trillion is not exceeded.

Mr. McGRATH. Can I break in here just for a second.

Dr. MILLER. Surely.

Mr. McGRATH. Having said all of that, if I were a gefilte fish manufacturer, with all of these statistics, could you in court substantiate your findings or your levels of concern?

Dr. MILLER. Yes.

As a matter of fact, it is usually the other way around. Usually if we do go to court someone is challenging the fact that we have been too conservative. We have to indicate that in fact that we have not been too conservative in this respect.

We think we have taken a very reasonable and conservative approach as well.

With your permission, Mr. Chairman, we have already in fact submitted, for the record, a description of the problems of the analytical methodology. I think this is keyed to where we go with this.

We have a description of the analytical methodology used to detect TCDD, and also included in that, some points about its difficulties; why it is so difficult. We have also included a table of some of the results we have obtained over the past 3 years on TCDD analyses in various parts of the country.

Mr. Chairman, I believe it is important to emphasize again that any estimate of an acceptable level of exposure to TCDD by human populations is clouded by many uncertainties.

Some of these uncertainties are the relative sensitivity of human populations to TCDD as compared to the animal species tested and the possibility that certain individuals within the exposed population are unusually susceptible to the adverse effects of TCDD. Such unusual susceptibility could derive from a host of factors including genetic background, dietary or nutritional status, exposure to other halogenated aryl substances, such as other dioxins and dibenzofurans, disease, and even other factors we have not even considered.

With these reasons it is important to keep in mind that if new information becomes available we will have to change our decisions.

Mr. Chairman, in your letter of invitation, you also asked what kind of information is required to increase the certainty of our regulatory judgment. Clearly, as we have indicated several times in our remarks, we need to know with much greater confidence the relative sensitivity of the human to TCDD.

This controversy has split the scientific and medical communities and its solution is essential to any rational regulatory action. To accomplish this task, we need not only to expand, focus, and refine our epidemiologic efforts, but also we need to better understand the mechanisms by which TCDD exerts its effects.

With such data, we can then determine the relationship of the involved metabolic pathways to those in man and should be able to identify specific metabolic endpoints with which the toxicity of TCDD can be monitored in man at levels of exposure that may not lead to overt chronic effects.

We also need to develop much more economic, rapid and specific methods of analysis that can accurately and precisely identify TCDD in foods at levels of concern. This would permit not only easier identification of products of concern, but more importantly,

would allow many more analyses of a greater variety of food products that we obtain from a large number of markets.

That completes any remarks that I would like to make, Mr. Chairman.

[The prepared statement of Dr. Miller follows:]

STATEMENT BY SANFORD A. MILLER, PH. D.

Mr. Chairman:

The Food and Drug Administration (FDA) appreciates the opportunity to testify on the human health effects resulting from exposure to 2, 3, 7, 8-tetrachlorodibenzodioxin (TCDD).

Since the Subcommittee is familiar with FDA's responsibility and jurisdiction over food products containing environmental contaminants, including dioxins, I will try to give primary emphasis to issues raised by the Subcommitte in its letter of invitation.

As we have heard from scientists from the National Institute of Environmental Health Sciences and the Centers for Disease Control, TCDD is a highly toxic compound which in certain animals causes birth defects, cancer, immunotoxicity, and a variety of biochemical and physiological alterations. Most of what is known about TCDD's toxicity derives from animal studies, particularly studies in rats, mice, and guinea pigs. It is evident that the sensitivity of different rodent species to TCDD varies greatly, perhaps by as much as a thousandfold. This information is important to keep in mind, since our ultimate task is to estimate safe levels of exposure to human populations. Unfortunately, based on current information, it is not possible to determine whether humans are more sensitive or less sensitive than the highly susceptible rodent species. The reason for this is that the exposure level to humans is very difficult to estimate accurately.

While there have been accidental exposures to TCDD, such as the Seveso, Italy incident, the actual levels of exposure to humans is unknown. There are scientists who have argued that humans are relatively insensitive to the effects to TCDD based on studies with

cohorts of individuals accidentally exposed to dioxin who have subsequently developed chloracne--the argument being that systemic exposure must have been significant for chloracne to have developed. The counter-argument states that chloracne might have been the result of topical exposure only where little of the compound penetrated the skin to expose the individual systemically. Hence, systemic effects would not be expected to be seen. Based on present knowledge, we cannot reliably state whether humans are more or less sensitive than the animal models that have been used to explore the toxicity of TCDD. Nevertheless, in recommending the concern levels for TCDD in Great Lakes fish at 25 and 50 parts per trillion (ppt), FDA has in effect acknowledged the extremely potent toxicity of TCDD as determined experimentally using animal models.

FDA's actions on another toxic substance, aflatoxin B_1, illustrates our concern for TCDD. Aflatoxin B_1, which is a metabolite of the mold Aspergillus flavus, has always been considered an extraordinarily toxic and carcinogenic substance. Because this mold grows naturally on peanuts and corn, particularly corn in the Southeastern United States, toxic levels of aflatoxin are impossible to avoid entirely. Consequently, the FDA, under the authority of section 406 of the Federal Food, Drug, and Cosmetic Act, has establish an action level for the presence of aflatoxin in food commodities and finished food products. The point here is that the action level established for aflatoxin is approximately 1,000 times higher than the concern level that FDA recommended to the Great Lakes States for TCDD residues in carp and catfish. It should be emphasized that prior to the findings on TCDD, aflatoxin was generally regarded as the most carcinogenic substance known to science.

In establishing either an action level or recommending a level of concern, FDA is both guided and constrained by its statutory authority. Under section 402(a)(1) of the Act, food is regarded as adulterated if it bears an added poisonous or deleterious substance at a level which may render that food harmful to human health at the levels consumed. If the substance in question is unavoidable by good manufacturing practice, section 406 provides for establishing a level which must protect the public health, while at the same time avoid needless reduction of the available food supply.

The Delaney clause, which states that no substance may be approved as a food additive if it is shown to induce cancer in man or animals, is a provision of section 409 of the Act and thereby applies to food additives, not to unavoidable contaminants in food. TCDD, in this instance, is not a food additive, but rather is an added poisonous or deleterious substance which cannot be completely avoided by good manufacturing practice. Therefore, TCDD in fish is subject to sections 402(a)(2) and 406 which do not contain a provision similar to the Delaney clause. Section 406 requires that the extent to which the poisonous or deleterious substance is unavoidable under good manufacturing practice be considered in setting a tolerance. Thus, in this sense FDA must determine the balance between health effects and the results to the consumer of removal of a food product from the market. This balancing is particularly difficult in the face of as much uncertainty as exists with TCDD. However, at the time we developed our recommendations, we were confident that they met both the requirement for public health protection, as well as avoided the needless reduction of part of the food supply.

We recognized then and recognize now, that there would be critics who would argue that the uncertainty of TCDD's health effects in humans and the knowledge of its high toxicity in laboratory animals would dictate that any level at which TCDD could be detected would be too high and that such food should be banned. This approach would, in fact, result in the banning of most bottom-feeding fish in the Great Lakes and possibly other species of fish, such as smelt. If the analytical methodology used for detecting TCDD improves by an order of magnitude, the likelihood is that still more species of fish would be found contaminated, resulting in the closing of those fisheries as well. Based on our evaluation of the available data, we felt that such action was not warranted and in our advisory stated that fish containing more than 50 ppt should not be consumed and those containing more than 25, but less than 50 ppt should not be consumed more than twice a month. We further stated that, based on fish consumption data, we saw no public health problem below 25 ppt.

It should be recognized that these values are not tolerances or action levels, but instead are levels of concern requested by several of the Great Lakes States affected by this problem. Since the Great Lakes are shared with Canada, we attempted to harmonize our concern with those of the Canadian Health Protection Board. We did not attempt to establish a tolerance for TCDD in fish as that would force FDA to formally prepare and defend the level. Such formal action on the part of FDA would be challengeable in the courts and we would need to defend the proposition that the fish were adulterated at the tolerance level by a poisonous and deleterious substance which may have rendered it harmful to <u>human</u> health under ordinary conditions of use.

On the other hand, FDA would also have to defend the proposition that below the action level there is no public health concern whatever.

Since there is considerable uncertainty about TCDD's effects on humans, particularly with regard to the question of the sensitivity of humans to various levels of TCDD, the Agency believed that any effort to set an action level or tolerance would be premature and possibly counterproductive. The concern level, which was developed primarily to provide guidance to the individual States that are confronted with the problem, reflected the apparently restricted nature of the food contamination in that it did not appear to be a national problem. For these reasons, the level of concern was believed preferable to an established action level or tolerance. It is important to note that this level was established only for the specific situation in fish in the Great Lakes, and does not apply to other foods or areas.

We arrived at the level of 25 ppt by examining the distribution pattern of TCDD in Great Lakes fish and then determined the risk associated with various levels of contamination. From our examination of the distribution of TCDD in fish in the affected area we concluded that, for the most part, the species of most concern were the bottom-feeding fish such as carp and catfish. Looking at the level of contamination and keeping in mind our statutory requirement to consider both public health and the availability of food, we evaluated several possible levels of concern ranging from 10 ppt to 100 ppt. We determined that 25 ppt represented a level of risk acceptable to the public health while resulting in a minimal impact on the availability of Great Lakes fish as a food source.

Let me now describe the basis for the Agency's conclusion that catfish and carp from the Great Lakes do not pose an unacceptable risk to the public health at a level of 25 ppt. According to the information available to us from food consumption surveys, the upper 90 percentile of fresh water fish consumption in the Great Lakes States is 15.7 grams of fish per day. For the United States as a whole, total fish consumption is about 28.1 grams per day. Most of this is marine fish which, insofar as is known, does not contain TCDD. Moreover, bottom feeders, such as carp and catfish, make up only a fraction of all fresh water fish.

Using the worst-case assumption that all exposed individuals consume high levels of fish (at the 90 percentile of fish consumption), that all the fish consumed are fresh water fish from contaminated areas in the Great Lakes, and that these fish consist exclusively of bottom feeders such as catfish and carp having exactly 25 ppt of TCDD, we calculated a daily exposure to TCDD of 392.5 picograms from such fish.

It should be kept in mind, however, that these exposure estimates are based on several assumptions that are most unlikely to hold true for even a single individual. For example, it needs to be recognized that to assure that no sample exceeds a 25 ppt residue level, the average limit imposed on any given fishery must be well below this and statistically would probably not exceed 1/3 of that amount. Thus, no individual would, on a consistent basis, consume fish at 25 ppt. Assuming that the individual consumed only bottom fish from the

Great Lakes fisheries, that person would probably consume fish with dioxin on the average of approximately 8 ppt. This then reduces the estimate of exposure to 130.8 picograms/day from such fish. Further, the average individual would not exclude consuming bottom fish from uncontaminated areas or surface-feeding fish with nondetectable levels of TCDD. In all likelihood, no more than 10 percent of the fish in the average individual's diet within the affected States is likely to be composed of bottom-feeding fish from contaminated areas. Taking this correction into account, the estimation of consumption is reduced to 13.1 picograms/day.

To determine the risks of cancer from this exposure, we utilized the best animal data available for the purpose which was developed by Kociba and his colleagues. We regarded these data as the best for the purpose of risk assessment, as this work provided the most information on the relationship of dose or exposure to response. Since the mechanism by which TCDD induces cancer in rodents is unknown, it is not possible to say which of the standard mathematical models are appropriate for use. We do assume, however, that most of these models are far more likely to overestimate risk, rather rather than underestimate it. Further, risk in this context says only that the data are consistent with the probability that the risk level could occur, not that it necessarily will occur. It also must be kept in mind that the relative sensitivity of humans to the animal models is not known and there is considerable controversy in scientific circles on this point.

With these caveats in mind, the risk levels represented by a 25 ppt maximum residue level representing a predicted exposure to an 80 kg

individual of approximately 13 pg/day is calculated as approximately 3 cancers out of a million or 3×10^{-6} lifetime risk using the linear model. Given the fact that the Agency viewed these "concern levels" as interim statements, it is important to consider what the lifetime risk of cancer might be for a specific increment of time. For a period of 1 year, the risk is 4 in 100,000,000 or 4×10^{-8} using the linear model. It should again be emphasized that these calculations make no pretense of representing an actuarial risk. The intent of the exercise is to obtain an estimate of the upper bound or upper limit of risk that a particular agent poses to exposed human beings. In this case, whether or not it represents an upper limit depends upon whether humans are less sensitive or more sensitive than the rodent models on which these estimates are based. Only time and the gathering of additional information will provide the insight necessary to adjust these estimates in whatever direction appears appropriate.

A further point needs to be made. At the present time, the concern level set at 25 ppt is consistent with the demands and the constraints imposed by the sensitivity of the analytical method used to detect TCDD. While there are analytical screening procedures which can detect TCDD at levels at approximately 1 ppt, these methods do not specifically identify TCDD. Confirmation that the chemical entity detected is in fact TCDD requires the use of specific mass spectroscopic techniques. In order to both detect and confirm TCDD, residue levels must be at least 10 ppt or higher. Therefore, in setting a level of concern, it was necessary that our chemists who monitor and analyze fish taken from the Great Lakes fisheries be able

to detect levels that were significantly below the level of concern in order to demonstrate the nature of the distribution of contamination in fish. As indicated earlier, to assure that fish containing levels of TCDD which exceed 25 ppt are not present, it is necessary to detect and measure with accuracy and precision, levels that are roughly 70 percent lower. In other words, the 25 ppt level of concern for Great Lakes bottom fish requires that the most sensitive method for detection and confirmation be used. This methodology is expensive. We estimate that it costs about $1,000 per sample. To set the concern level much lower than 25 ppt would be in fact be forcing the technology beyond its current state-of-the-art and would not provide a rigorous scientific basis for legal actions that might be taken.

I would like to provide for the record a description of the analytical methodology and some points about its difficulties that are relevant here. I would also like to submit some data on the levels of TCDD found in fish and other foods analyzed by our various laboratories.

As mentioned earlier, we indicated that should samples of fish exceed 25 ppt, such fish should not be consumed any more frequently than twice a month. We were asked for an advisory because of the possibility that people living along the Great Lakes might depend on these fish to provide a significant portion of their diet. At 50 ppt or over, we advised that there be no consumption. This statement is based on estimates of monthly exposure and is consistent with and does not exceed the estimates of the upper limit of risk calculated for 90 percentile consumption of fish at 25 ppt.

It is important to emphasize that any estimate of an acceptable level of exposure to TCDD by human populations is clouded by the following uncertainties: the relative sensitivity of human populations to TCDD as compared to the animal species tested and the possibility that certain individuals within the exposed population are unusually susceptible to the adverse effects of TCDD. Such unusual susceptibility could derive from a host of factors including genetic background, dietary or nutritional status, exposure to other halogenated aryl substances, such as other dioxins and dibenzofurans, disease, and possibly other predisposing factors. In this case, as in the case with many chemicals, the total information available does not provide full confidence for setting levels of concern or action levels. We are therefore compelled to rely upon the best data available and to make the most reasoned judgments possible within the framework of existing legislation. The decisions on TCDD are an example of this, but it is important to keep in mind that as new information becomes available, the decisions will change accordingly.

Mr. Chairman, in your letter of invitation you also asked what kind of information was required to increase the certainty of our regulatory judgments. Clearly, as we have indicated several times in our remarks, we need to know with much greater confidence the relative sensitivity of humans to TCDD. This controversy has split the scientific and medical communities and its solution is essential to any rational regulatory action. To accomplish this task, the scientific community in general needs not only to expand, focus and refine our epidemiologic efforts, but also needs to better understand the mechanism by which

TCDD exerts its effects. With such data, we can then determine the relationship of the involved metabolic pathways to those in man and should be able to identify specific metabolic endpoints with which the toxicity of TCDD can be monitored in man at levels of exposure that may not lead to overt chronic responses.

The scientific community also needs to develop more rapid and specific methods of analysis that can accurately and precisely identify TCDD at levels of concern. This would permit not only easier identification of products of concern, but more importantly, would allow many more analyses of a greater variety of food products obtained from a large number of markets.

In conclusion, Mr. Chairman, this example in regulatory decisionmaking illustrates FDA's role in protecting public health by ensuring a safe and nutritious food supply. This responsibility is exercised by individuals who call upon science, law, and the regulatory process to accommodate the demands of safety, contamination, food requirements, Congress, consumers, and the courts. Although the regulatory process has often been criticized, on the whole it has provided effective public health protection for the millions who consume food in the United States.

Mr. Chairman, this ends my formal statement. My colleagues and I will be happy to answer any questions you may have.

Mr. SCHEUER. Thank you, Dr. Miller.

Now we will hear from Dr. Donald Barnes, Senior Science Adviser to the Assistant Administrator for Pesticides and Toxic Substances, U.S. Environmental Protection Agency.

STATEMENT OF DR. DONALD BARNES, SENIOR SCIENCE ADVISER, OFFICE OF PESTICIDES AND TOXIC SUBSTANCES, ENVIRONMENTAL PROTECTION AGENCY –

Dr. BARNES. I have my prepared remarks as you have indicated. As I understand they will be entered into the record. I would just like to summarize certain points of them.

Mr. SCHEUER. Summarize informally in 6 or 8 minutes or 10 minutes. That would be fine.

Dr. BARNES. All right. I will do so.

Our testimony this morning focuses on 2,3,7,8-TCDD, only one of the 75 chlorinated dibenzodioxins thought to be the most toxic of the species. Although other chlorinated dibenzodioxins are present in the environment and are being addressed, most of the public attention has been focused on this particular congener.

My remarks are divided into three different areas. I will not focus on all of these at this time. The first portion deals with the EPA's history of dealing with dioxin in the environment which has spanned over a decade. We have taken certain regulatory actions and made decisions on this.

Then there is the section that deals with the potential health effects that we have encountered in these cases. Then there is a description of the research that we proposed that needs to be conducted for filling in the gaps in the data base that we presently have.

Then follows a discussion of the toxicity of the compound which sort of repeats what others have said before this committee and earlier.

We then have a discussion where we talk about how EPA has used this information on health effects to actually make decisions. That is really what we are concerned about.

The risk that has been presented by any given chemical is a function of its hazard, that is its inherent toxicity, and its exposure. Now the hazard information we get primarily from animal data that has been generated over the years.

The decisionmaking process turns in most cases upon the exposure that is associated with any particular instance. That is where we have focused much of our attention.

The effects of concern that we have looked at have been cancer and reproductive effects primarily. There is a discussion here of how we have utilized that analysis, which is not that much different from what the FDA and CDC have done in terms of the general approach.

In a typical 2,3,7,8-TCDD related situation, the Agency scientists provide decisionmakers with the results of a risk assessment. This risk assessment is generally produced in a spectrum of risks as a function of concentration, let's say, TCDD and the soil.

This is where the scientific aspect, if you will, changes from risk assessment, and the idea of risk management takes place.

The distinction between risk assessment and risk management has been highlighted in a recent National Academy of Sciences report entitled, "Risk Assessment in the Federal Government." Generally risk assessment is an objective, scientific evaluation of the magnitude of the risk independent of considerations of what should be done about that risk. Risk management is the decision-making process involving more subjective societal judgments which consider certain nonrisk factors when selecting an appropriate response to that risk.

In a speech delivered last month before the National Academy, Administrator Ruckelshaus emphasized this difference, indicating that the two processes, risk assessment and risk management, should be separated within a regulatory agency.

In his letter of invitation to these hearings, the subcommittee has asked EPA specifically what evidence on the affect of dioxin on human health justifies establishing a dioxin concentration standard of one part per billion in soil, and how should such a standard be interpreted and used.

I believe your question may have been prompted by EPA's recent relocation action under Superfund. EPA welcomes the opportunity this hearing affords to clarify what has erroneously been characterized in some press reports as EPA's safe level of dioxin.

First of all there is no simple level which can give rise to risk that is equivalent in all cases. Even if one were to decide upon an acceptable level of risk, the key question of exposure must be addressed on a site specific basis before any estimate of an acceptable level of contamination in the soil can be made.

For example, a decisionmaker could conclude that greater than a part per billion of 2,3,7,8-TCDD in the soil of one person's front yard might represent an unreasonable risk since such a person might not be expected to easily or reasonably limit his exposure to this soil.

That same decisionmaker could conclude, however, that many times that level is acceptable in an isolated spot of a manufacturing site or at the bottom of a reclaimed dumpsite where people are unlikely to be exposed.

In sum, the determination of an acceptable level is dependent upon many factors, and it is an oversimplification to seek for a universally applicable level.

Second, the act of establishing a level is no longer in the realm of risk assessment. Instead this is the province of risk management. In assessing risks, scientists can, for example, present the decisionmaker with a graphical summary illustrating the possible range of risks associated with various exposure scenarios and contamination levels in the soil.

In reaching the risk management decision, the decisionmaker weighs all of the elements in the risk assessment. He weighs the strength of the qualitative case, the exposure assessment, the limitations, and the uncertainties involved.

In addition, the decisionmaker factors in nonrisk considerations which might include feasibility and cost of cleanup, possible alternative actions, consistency with regulation of other risks, and concerns of the affected community.

In sum, while the scientists may agree that a certain spectrum of risk is associated with different levels of contamination and exposure, precisely where on that spectrum a decisionmaker determines the appropriate level will vary as factors specific to a given situation are considered.

Thus, EPA has not adopted general applicable action levels for Superfund purposes. Rather, the Agency continues to make decisions on a site-by-site basis, taking into consideration both the CDC health advisories and any special onsite circumstances in determining action at individual sites.

Finally, I would like to address some of the gaps in our knowledge about the toxicity of TCDD and the environment, and what type of research would improve the scientific data base. Then, I will follow with a list of specific items. I would just like to highlight a couple.

One is the toxicity as it is affected by other media, or its presence in specific media. Most of the studies to date have been done on dioxin, if you will, native dioxin administered to animals.

However, when we are in the environment we find dioxin attached to soil particles, in fish, and so on. Studies with dioxin in this particular form have not been done.

EPA is critically interested in trying to figure out what you do with dioxin once you find it. Destruction and disposal techniques need to be further researched.

Reiterating something that Dr. Miller had mentioned and that we feel strongly about, is mechanism-of-action studies and pharmacokinetics. Important information is currently being deduced about the first stages of toxicity induced by 2,3,7,8-TCDD and related compounds.

As we obtain more fundamental knowledge about what is happening at the molecular and cellular levels, the possibility of our being able to understand exactly how and why 2,3,7,8-TCDD exerts its toxicity increases.

This information may help us explain the basis of the species variability of where humans fall in this range of reaction. Moreover, we may then be able to assess the toxic potential of literally hundreds of related toxic chemicals without devoting to each individual chemical the mass of resources we have had to dedicate to 2,3,7,8-TCDD.

As a final word, I would like to observe that it is important that we keep the dioxin problem in a proper perspective. I believe we need to address the dioxin issue in a rational and deliberate manner. At the same time we should not permit this legitimate concern to cause us to neglect other legitimate concerns such as those embodied in the pools pits, and lagoons of abandoned dumpsites, the emission of toxic pollutants into our air and water, and the potential for unreasonable risks associated with chemicals to which we are exposed daily.

As scientists and regulators, we have an obligation to maintain a balance among all of these concerns.

This concludes my prepared testimony. I would be happy to answer any questions that you might have regarding these matters.

[The prepared statement of Dr. Barnes follows:]

STATEMENT OF DR. DONALD BARNES

Good morning, Mr. Chairman and Members of the Subcommittee. I am Donald Barnes, Science Advisor to the Assistant Administrator for Pesticides and Toxic Substances of the Environmental Protection Agency. Since 1980, I have been chairman of the Agency's Chlorinated Dioxins Work Group, which has been assisting in the coordination of the Agency's involvement in dioxin-related matters. In addition, I have represented the Agency on the Cabinet Council's Agent Orange Work Group, chaired by the Department of Health and Human Services.

My testimony this morning focuses on 2,3,7,8-tetrachloro-dibenzo-p-dioxin (2,3,7,8-TCDD), what is generally considered to be the most toxic of the 75 chlorinated dibenzo-p-dioxins (CDDs). Although other CDDs are present in the environment and are being addressed, most public attention is being focused on this particular dioxin. My remarks are divided into three sections. In the first, I will briefly describe some of the situations in which EPA has been involved with 2,3,7,8-TCDD in the environment. Next, I will discuss the data and the methods we have used to assess the potential for human health effects in these cases. Finally, I will describe some of the gaps in our knowledge about 2,3,7,8-TCDD and the research that would help fill those gaps.

EPA first became aware of the hazards associated with 2,3,7,8-TCDD through laboratory animal studies conducted in the 1960s and early 1970s. At that time, the scope of the Agency's "dioxin problem" was defined by the presence of 2,3,7,8-TCDD as an unavoidable contaminant in certain pesticide products. During the 1970s, the Agency took action to restrict the use of certain of these pesticide products and to obtain more information about the toxicity of 2,3,7,8-TCDD and analytical methods for detecting its presence in the environment. Some of these efforts involved extensive cooperation between EPA, various academic institutions and environmental groups, other Federal agencies, and industry. By the end of the decade, this cooperative venture had succeeded in developing a method to reliably detect TCDD in some media in the low parts per trillion range. (One part per trillion is roughly equivalent to the thickness of a human hair compared to the distance across the United States.)

In 1979, based on extensive animal data and epidemiologic information, the Agency took emergency action to suspend certain uses of 2,4,5-T and Silvex, two pesticide products which contain 2,3,7,8-TCDD. That ban remains in effect at this time.

Also in the late 1970s, the Agency took action in connection with a series of dumpsites along the Niagara River in New York, some of which were found to contain 2,3,7,8-TCDD wastes. These wastes were found along with a range of other hazardous substances which had resulted from previous manufacturing operations in the area. During the same time period, the Agency provided technical assistance in the successful cleanup of a smaller dioxin contaminated dumpsite in Missouri.

By 1979, the possibility of a range of dioxin emissions from combustion processes had become an issue. During this period, the Agency carefully investigated the question of the emission of 2,3,7,8-TCDD, other TCDD isomers, and tetrachlorinated dibenzofurans (TCDFs) during the combustion of polychlorinated biphenyls (PCBs) at two hazardous waste incinerators in the midwest.

In 1980 and 1981, the Agency participated on a United States team, headed by the Food and Drug Administration (FDA), which met with Canadian officials to determine the presence of 2,3,7,8-TCDD in fish in the Great Lakes, assess the significance of these findings, and discuss ways to reduce or remove any sources of contamination.

In 1980, the Agency issued a rule that requires 60-day notification to EPA prior to the disposal of most 2,3,7,8-TCDD contaminated manufacturing wastes. This 60-day period gives the Agency the opportunity to assess the risks associated with the proposed disposal and to take action if those risks are judged too unreasonable.

In 1981, furthering its assessment of the emissions from combustion processes, EPA completed a series of studies of TCDD emissions during the combustion of municipal wastes. TCDDs, including small amounts of 2,3,7,8-TCDD, were detected at four of five facilities sampled. An interim evaluation of the significance of these TCDD emissions for human health was issued in November, 1981, and concluded that the emissions "do not present a public health hazard for residents living in the immediate vicinity" of the facilities tested.

More recently, the Agency has been active in indentifying sites in several states, predominately in Missouri, which have been contaminated with 2,3,7,8-TCDD as a consequence of manufacturing activities or the injudicious disposition of wastes.

Finally, I would like to mention that an EPA Task Force on Dioxins, with representatives from several program offices, is currently developing an overall strategy

which will recommend specific actions and coordination mechanisms to address the wide range of dioxin questions. The top management at EPA now have this strategy under review.

I have included this chronology neither to seek commendation nor to evoke sympathy, but rather to illustrate that the Agency is no stranger to 2,3,7,8-TCDD and the challenge it presents to those required to make decisions regarding unreasonable risks to human health and the environment.

The data base on 2,3,7,8-TCDD toxicity is extensive, but certainly not exhaustive. Much of what we know has been obtained from animal studies. For example, we know that the material is lethal to a variety of animal species when administratered in single, small doses (less than a millionth of a gram in some species). We know that there is a 1000-fold range of toxic response among various species in these lethality studies. We know that 2,3,7,8-TCDD is carcinogenic in rats and mice at very low doses (via both ingestion and dermal absorption), resulting in a variety of tumors in these animals. We know that, as a carcinogen, it can at least behave as a promoter, a compound capable of eliciting frank carcinogenesis in animals which have been previously exposed to other carcinogens, and as a cocarcinogen. We know that the compound can interfere with reproductive success in females, especially pregnant ones, of several species (including rats, mice, rabbits, and monkeys), often at very low doses. We know that the material can affect elements of the immune system in test animals. In addition, there are a number of other effects which have been observed, including organ damage (for example, to the liver and thymus), metabolic disruptions, and significant enzymatic changes.

In the area of human health effects, our folder of known information is somewhat slimmer. This is partially due to the fact that most human data are obtained from occupational exposure and industrial accidents. In these cases, it has been difficult to estimate the level of 2,3,7,8-TCDD exposure in individual cases or to distinguish the effect of concommitant exposure to other chemicals. In any event, there is general agreement in the scientific community that chloracne, a persistent, acne-like condition which can be disfiguring but which is not life-threatening, is associated with persons acutely exposed to 2,3,7,8-TCDD. Chloracne can also be evoked by a number of chlorinated hydrocarbon chemicals in addition to 2,3,7,8-TCDD. Other effects which have been associated with these exposure incidents, and which are generally considered to be short-term, include liver dysfunction, effects on the immune system, and various neurological complaints.

A series of reports has associated human exposure to 2,3,7,8-TCDD containing chemicals and a rare form of cancer, soft tissue sarcoma. This possible link was first reported in a pair of studies of Swedish workers, and additional, but not definitive, support for the association was found by re-assessing studies completed here in the United States, in which isolated cases of soft tissue sarcomas have been found in 2,3,7,8-TCDD exposed populations. However, other studies both here and abroad have failed to confirm this association. This possible association is being explored in a number of current or planned studies by various government agencies.

In considering risk, one must remember that risk is a function of two variables: hazard and exposure. A reduction in the size of either variable will result in a comparable reduction in risk. For example, even the most hazardous substance will be of no risk, if its exposure to people and the environment can be reduced to zero. In evaluating risk, the Agency combines hazard information (data on inherent toxicity) and exposure data to arrive at quantitative estimates of risk. To illustrate, I will briefly discuss how the Agency assesses carcinogenic and reproductive effects.

The Agency assesses the excess risk of cancer using the methods of the Cancer Assessment Group (CAG), whose guidelines were published in 1976. Briefly, the Agency first examines the data base to make a determination as to whether the chemical substance is a carcinogen. In addition to the qualitative question, a quantitative extrapolation to low environmental doses is performed in order to estimate a rough upper bound for the risk, using a linear, non-threshold procedure. This presumes that the initiation of cancer is a non-threshold phenomenon; that is, there is some risk, perhaps very small, at any exposure above zero. In the case of 2,3,7,8-TCDD the Agency has based its quantitative analysis primarily on the linearized, multi-stage extrapolation model, although several others have also been used on occasion. It should be pointed out that these procedures result not in an absolute prediction of the risk, but rather a "ballpark" estimate of the upper limit of risk which we do not believe will be exceeded. The actual risk is likely to be some value less than this upper limit, possibly zero. These extrapolation procedures indicated that 2,3,7,8-TCDD was quite potent compared to many other carcinogens evaluated using the same techniques.

32-911 O—84——7

The magnitude of the risk depends heavily on the level of 2,3,7,8-TCDD to which people are exposed and the likelihood that this exposure results in an absorbed, toxicologically active dose. Usually, we do not have definitive information on human exposure. In lieu of such data, the Agency makes certain assumptions, usually of the "reasonable worst case" variety, so as to err on the side of public safety. For example, in the case of TCDDs emitted from combustion sources, the Agency assumed that a person might spend his entire life at the spot of highest estimated ground level concentration, that all TCDDs inhaled would be retained, and that TCDDs attached to particles would be completely biologically active. "Reasonable worst case" estimates of exposure, when combined with the extrapolation results, lead to an estimate of the upper limit of risk.

In contrast to cancer, the Agency has generally regarded reproductive hazard as one for which there exists a level of exposure below which it is not expected that an adverse effect will occur, the so-called "threshold assumption." In assessing this type of risk, the scientist uses an adequate study in which an administered dose level resulted in no observed adverse effects (NOAEL) in test animals and compares it to the generally smaller level of estimated human exposure. The ratio of the NOAEL to this estimated human exposure is referred to as the margin of safety.

In the case of 2,3,7,8-TCDD, the Agency used a study in which rats were followed over three generations to determine the effect of 2,3,7,8-TCDD on the reproductive success of the animals. Although the authors of the study reported that no consistent adverse effects were observed at the lowest dose tested, EPA scientists concluded that statistically significant effects were observed at that dose and that the study lacked sufficient statistical power to conclusively demonstrate a NOAEL. This issue has been the source of considerable debate. Therefore, in comparing the lowest dose tested to the estimated exposure dose in humans, the Agency speaks of a "confidence ratio," instead of a "margin of safety."

In recent decisions associated with the Comprehensive Environmental Response, Compensation and Liability Act (CERLA, or "Superfund"), the Agency has also made use of risk evaluations generated by the Centers for Disease Control (CDC). In general, CDC uses methods which are comparable to those of the Agency.

In a typical 2,3,7,8-TCDD related situation, Agency scientists provide decisionmakers with the results of a risk assessment; i.e., estimated upper limits of cancer risk and confidence ratios for reproductive effects associated with various exposure scenarios. The assumptions and limitations of the approach should be explicitly stated. At this point, risk assessment ends and risk management begins.

The distinction between risk assessment and risk management has been highlighted in the recent report of the National Academy of Sciences (NAS) entitled Risk Assessment in the Federal Government. Generally, risk assessment is an objective, scientific evaluation of the magnitude of the risk, independent of considerations of what should be done about that risk. Risk management is the decisionmaking process, involving more subjective, societal judgments which consider certain non-risk factors when selecting an appropriate response to the risk. In a speech delivered last week at the NAS, EPA Administrator Ruckelshaus emphasized this difference, stating that the two processes should remain separated within a regulatory agency.

In its letter of invitation to these hearings the Subcommittee has asked EPA specifically, "What evidence on the effects of dioxin on human health justifies establishing a dioxin concentration standard of one part per billion in soil and how should such a standard be interpreted and used?" I believe your question may have been promoted by EPA's recent relocation action under "Superfund," and EPA welcomes the opportunity this hearing affords to clarify what has been erroneously characterized by some press reports as an EPA "safe" level of dioxin.

First of all, there is no simple level which will give rise to equivalent risks in all cases. Even if one were to decide on an acceptable level of risk, the key question of exposure must be addressed on a site-specific basis before making any estimate of an acceptable level of contamination in the soil. For example, a decisionmaker could conclude that greater than 1 ppb of 2,3,7,8-TCDD in the soil of one person's front yard might represent an unreasonable risk, since such a person might not be expected to easily or reasonably limit his exposure to this soil. That same decisionmaker could conclude, however, that many times that level is acceptable in an isolated spot at a manufacturing site or at the bottom of a reclaimed dumpsite where people are unlikely to be exposed. In sum, the determination of an acceptable level is dependent upon many factors, and it is an oversimplification to seek for a universally applicable level.

Second, the act of establishing a level is no longer in the realm of risk assessment; instead, this is the province of risk management. In assessing risks, scientists can,

for example, present the decisionmaker with a graphical summary illustrating the possible range of risks associated with various exposure scenarios and contamination levels in the soil. In reaching the risk management decision, the decisionmaker weighs all the elements of the risk assessment; i.e., the qualitative case, the quantitative case, the exposure assessment, and the limitations and uncertainties involved. In addition, the decisionmaker factors in non-risk considerations, which might include feasibility and cost of clean-up, possible alternative actions, consistency with regulation of other risks, and concerns of the affected community. In sum, while the scientists may agree that a certain spectrum of risk is associated with different levels of contamination and exposure, precisely where on that spectrum a decisionmaker determines the appropriate level to be will very as factors specific to a given situation are considered.

Thus, EPA has not adopted a generally applicable action level for "Superfund" purposes; rather the Agency continues to make decisions on a site-by-site basis, taking into consideration both the CDC health advisories and any special on-site circumstances in determining action at individual sites.

Finally, I would like to address some of the gaps in our scientific knowledge about toxicity of 2,3,7,8-TCDD in the environment and what type of research would improve the scientific data base for decisionmaking.

1. Toxicity of 2,3,7,8-TCDD in complex mixtures—Most of the data generated to date has been with 2,3,7,8-TCDD alone. In the environment, however, we usually encounter the compound in combination with other materials and associated with particulates; e.g., soil or fly ash. The effects of dioxins in the presence of these other materials need to be investigated to answer questions of synergism and bioavailability. Promising techniques for assessing "TCDD equivalents" of such complex mixtures should be developed further.

2. Exposure issues—We need to know more about the ways 2,3,7,8-TCDD moves in the environment; e.g., possibility of volatilization, bioaccumulation from soils into fish, dermal penetration, and the amount of soil children might ingest.

3. Disposal/destruction methods—Currently, adequately tested and practical methods for disposal and/or destruction of dioxin contaminated materials are limited. Much work remains to be done to determine how best to deal with this material once it has been discovered in the environment.

4. Epidemiological studies—Various Federal agencies are now conducting epidemiological studies to investigate the possible effects of 2,3,7,8-TCDD in humans. There are additional studies which could be conducted, involving populations near more recently discovered contamination sites.

5. Background levels—It would be helpful to know the background level of 2,3,7,8-TCDD in various parts of the environment, such as land, various foods, and human tissue. This information could serve as valuable benchmarks.

6. Related compounds—There are 74 other chlorinated dibenzo-p-dioxins and 135 chlorinated dibenzofurans, some of which are also of concern and appear in the environment. Activities need to be encouraged to deal with these compounds on a rational, deliberate basis.

7. Mechanism-of-action studies and pharmacokinetics—Important information is currently being deduced about the first stages of toxicity induced by 2,3,7,8-TCDD and related compounds. As we obtain more fundamental knowledge about what is happening at the molecular and cellular level, the possibility of our being able to undestand exactly how and why 2,3,7,8-TCDD exerts its toxicity increases. This information may help us explain the basis of the species variability and where humans fall in this range of reactions. Moreover, we may then be able to assess the toxic potential of literally hundreds of related toxic chemicals without devoting to each individual compound the mass of resources we have had to dedicate to 2,3,7,8-TCDD.

As a final word, I would like to observe that it is important that we keep the dioxin problem in a proper perspective. I believe we need to address the dioxin issue in a rational, deliberate manner. At the same time, we should not permit this legitimate concern to cause us to neglect other legitimate concerns, such as those embodied in the pools, pits, and lagoons, of abandoned dumpsites, the emission of toxic pollutants into our air and water, and the potential for unreasonable risks associated with chemicals to which we are exposed daily. As scientists and regulators, we have an obligation to maintain a balance among all of these concerns.

This concludes my prepared testimony. I would be happy to answer any questions you might have regarding these matters.

Mr. SCHEUER. Thank you very, very much, Dr. Barnes.
Here is Congressman McGrath of New York.

Mr. MCGRATH. First of all, Dr. Miller, how many agencies are presently conducting experimentation into dioxin?

Dr. MILLER. I do not know offhand exactly how many, Mr. McGrath. But I suspect that there are at least a half a dozen that are doing research in one area or another.

Mr. MCGRATH. Is there a mechanism for a core group to share information to determine the manner in which this experimentation should be taking place?

Dr. MILLER. Yes.

Dr. Barnes of EPA has been involved in the organization of these activities. Perhaps I will let him respond to your question.

Mr. MCGRATH. My question is prompted by the fact that CDC establishes a one part per billion in soil, FDA a 25 parts per trillion in a certain other thing, and now the EPA has another standard for something else. It seems to me that it is scattered somewhere all over the place.

Dr. MILLER. No, no. I think I know where the problem comes from. But actually they are all based on the same assumptions.

There is a convergence of views on this subject. There was a meeting recently in Atlanta on issues like this.

The fact of the matter is is that in each case the primary issue, as Dr. Barnes pointed out, is exposure. How much actual amount are people exposed to. And the amount that is set for whatever place it is, whether it is Time Beach or someplace else, is based upon the assumption of a certain level of exposure.

CDC estimated, at their one part per billion, that people would be exposed to, at the lower level around a hundred parts per trillion, a 100 picograms per day of TCDD, or 25 parts per trillion. Our estimate gives us approximately the same level of exposure and so on.

The level which we set is in part based upon how often people are going to be exposed, whether it is in soil, or whether it is in fish, whether it is in water, and how available it is. The actual number may differ. But the bottom line is actually how many molecules of TCDD are people going to be exposed to. That is about the same.

Mr. MCGRATH. All right.

In your best judgment in talking about risk assessment, which is more risky, for me to smoke this cigar, because of the dioxin that is emitted from the cigar, or for me to eat three gefilte fish?

Dr. MILLER. As far as I am concerned that cigar represents a hazard not only to you perhaps but perhaps to Mr. Scheuer sitting next to you as well.

Mr. MCGRATH. He just asked me for one. [General laughter.]

But the point is, it is a risk that I wish to assume.

Dr. MILLER. This is the reason why from a regulatory point of view in attempting to set these levels, the agency is as conservative as it possibly can be because it is not an assumed risk.

We set these levels making our risk assessments. Our regulatory strategies are based upon the most conservative view. Usually we are challenged on the basis that we are too conservative. We have overestimated the risk. That is probably correct.

Nevertheless we feel compelled because they are not assumed risks that we have to work at the lowest possible level.

In the case of something like the TCDD, we are talking about something which the law, I think, correctly says. We also have to keep in mind that we do not want to destroy a substantial portion of the food supply. We have a responsibility for keeping that there, too.

We set it as low as we can. We are at the point where we are using conservative estimates. We are as certain as we can be that the risk is trivial, it is low. You never can say it is zero. At the same time we are not challenging a substantial portion of the food supply. I think that is what we have done in this case.

Mr. McGRATH. Thank you, Mr. Chairman.

Mr. SCHEUER. Congressman Volkmer.

Mr. VOLKMER. Dr. Barnes, under the new HUD independent agency appropriation bill, there is provided in there funds for additional research for health effects of dioxin, and I believe also for degradation.

In reading your statement I assume, I guess rightfully so, that EPA does see the need for additional research in both areas?

Dr. BARNES. The items that I have listed in my testimony indicate those areas where we feel additional knowledge is needed, yes.

Mr. VOLKMER. Will we see, then, additional research in the future by EPA on methodology of possibly speeding up natural degradation of dioxin?

Dr. BARNES. There is some work underway already in that area. We see the need that we need to do more in that area.

Mr. VOLKMER. We did make a mistake several years ago, did we not, in estimates of the natural degradation of dioxin?

Dr. BARNES. It had originally been determined by scientific data at the time that it looked as though the material would hang around for only about a year once it was in the soil.

Mr. VOLKMER. Yes.

Dr. BARNES. We have now found that that was a mistake. It looks like it will hang around for at least 10 years.

Mr. VOLKMER. All right.

Now on the health effects, how do you plan to do further research on the health effects of dioxin?

Dr. BARNES. Well, there is——

Mr. VOLKMER. Do you plan to just follow up people that have been exposed to it, et cetera?

Dr. BARNES. Certainly that is one area that needs to be addressed. We need to identify populations that may have been exposed. Fortunately, we believe that those are limited in extent. That not many people have been exposed to large amounts of dioxin. Therefore, that makes epidemiological studies difficult to conduct.

We certainly feel as though we need to do that. But there are additional studies that we can do with animals to determine the toxicity of dioxin as it appears in the environment.

As I indicated earlier in my testimony, much of the work to date has been done on just giving them straight dioxin, if you will.

Mr. VOLKMER. Right.

Dr. BARNES. Right now there is a study underway at the national toxicology program, for example, of feeding guinea pigs Missouri soil that has been contaminated with dioxin.

They have been given doses, which if that dioxin is biologically available, just as it would be if you gave it to them straight, they will belly up pretty quick. It may turn out that the fact that it is on soil means that it being retained. It is not available to the organism. Therefore they will not die as rapidly or nearly as much.

We will have a measure then of how the presence of the soil mitigates or changes the toxicity of this material.

Mr. VOLKMER. Thank you, Mr. Chairman.

I do not have any additional questions.

Mr. SCHEUER. This is a rollcall vote. I stayed here through the quorum call. But a rollcall vote we all must answer.

With your indulgence I am going to declare——

Mr. VOLKMER. By name.

Mr. SCHEUER. I know that.

Mr. VOLKMER. The machine is out of order, so it will take a little more time.

Mr. SCHEUER. So, it will take a little bit longer, maybe 15 or 20 minutes. With your indulgence we will come back. We will have a few questions for you.

We will recess for about 20 minutes.

[Recess taken.]

Mr. SCHEUER. The committee is reconvened.

Let me read to you a few paragraphs of learning for which we are indebted to the American Medical Association.

Whereas, dioxin occurs in many forms, some non-toxic and another said to be the most powerful toxin known to man.

And whereas, from the same study it is evident that no one knows or can truthfully say what level of body dioxin or environment dioxin is dangerous to humans.

And whereas, the news media have made dioxin the focus of a witch hunt by disseminating rumors, hearsay and unconfirmed, unscientific reports, including quotes attributed to scientists whose quote should have been, "I don't know".

And whereas, the lives and well-being of many inhabitants of the regions contaminated with dioxin have been unnecessarily and ignorantly damaged by this hysterical malreporting.

And whereas, the AMA and all members of the medical profession have a duty to speak loudly when their patients are repeatedly frightened by this wave of hysteria.

Therefore be it resolved that the AMA institute an active public information campaign to get accurate information on dioxin before the public to prevent irrational reaction and unjustified public fright and to prevent dissemination of possible erroneous information.

You can see how important it is for us to continue our deliberations here today in the most thoughtful and contemplative, moderate fashion.

Do you all agree to that?

Dr. MILLER. I don't know how you can disagree with the need to develop more information. On the other hand to imply somehow that this is not an important public health problem is probably worse than overestimating.

I think our attitude has been from the beginning is that it is a problem that needs to be examined carefully. It needs to be looked at rationally. But at the same time one has to accept the fact that this is a very potent toxic material and we have to deal with it.

Dr. BARNES. Just to reiterate, we look at dioxin as almost exquisite in terms of its properties. It is exceptional. In that regard I think it needs to have exceptional attention.

Mr. SCHEUER. Just being a devil's advocate for a moment, the advocatus diaboli, you say that the dioxin is exquisite. Yet nobody has educed any evidence, and Dow Chemical says this repeatedly, that dioxin has any more serious human health effects than chloracne.

They say that dioxin comes every time you broil a beefsteak or a steak over a charcoal fire. You are emitting dioxin that comes from combustion, and it has been around for thousands of years. What are we all getting so excited about?

If the medical profession has no evidence of harm to humans from dioxin, over and above chloracne, why are we going through this process that is getting people concerned and upset.

I am suggesting that this is more or less the position of Dow Chemical Co., and apparently the position of the AMA.

Dr. BARNES. Well, certainly that's part of its exquisiteness, if you will, is the fact that it demonstrates its toxic effects so clearly and at such low levels in animals. And we have such little evidence in the human sphere.

Traditionally, rational toxicology has always dictated that we learn from animal experience, and do not wait for human experience to dictate whether or not we take any action.

Therefore, this is a clear signal that we ought to be looking very carefully, which I think we are doing. As Dr. Miller says, there is more to know.

On the other hand, the material has not, if you will, fulfilled its worst conceivable reputation.

Mr. SCHEUER. Its worst case potential.

Dr. BARNES. Its worst case potential has not evolved. Now, whether that's just through the goodness of God that that's the case, we don't know. We would like to know more.

Dr. MILLER. I think there is another point, too.

I think the statement that dioxins, or TCDD in particular, and the other dioxins have been with us since, you know, the first volcanoes starting spewing out, is probably correct.

But like everything else it is a matter of dose. How much are you exposed to? I think we can be pretty well sure that when the volcanoes were spewing out dioxins, the amount that was showing up in our water supply and so on and where fish would swim and so on, is considerably less than that which is coming out of our plants and are contaminating those water supplies.

Mr. SCHEUER. Talking about emanations from plants, is the Dow Chemical Co. still refusing to give EPA access to its plant in Midland, Mich., in order to study the apparently dioxin laden discharges into the Tittabawassee River?

Dr. BARNES. Dow has indicated that they are moving forward on a good faith effort to answer these kinds of questions. There is a discussion that will be held in August which will look at the whole range of Dow related and EPA related dioxin issues.

This would include Dow's proposal for a $3 million study, and possible joint participation to some degree in that, and the detailed access to the detailed kinds of information that the Agency has recommended.

At this point, I guess the position of the Agency is that we feel as though there is a good faith commitment on the part of Dow to

follow through and provide the kind of information that we think is necessary.

Mr. SCHEUER. And provide what?

Dr. BARNES. And provide the kind of information that we think is necessary.

Mr. SCHEUER. They have said they would do that? Have they put that in writing?

Dr. BARNES. I don't know. I was just talking with the people in our Chicago office, and what I've just said orally is their impression. They have scheduled a meeting for August, and they feel as though things are moving along at this point.

Mr. SCHEUER. Yes.

I would like you to make sure this committee is kept informed of the progress of those negotiations. We would like to get a copy of any memorandum of understanding or any contract or any letter of intent, whatsoever the form it may take, whenever that is signed.

Dr. BARNES. Right.

Mr. SCHEUER. Are you satisfied that they are moving diligently to protect the public interest as expeditiously as possible?

Dr. BARNES. I am not familiar with all the details, but the fact that our regional office feels as though we are now moving in the right direction gives me confidence that that is the case.

Mr. SCHEUER. Yes.

There is no doubt that there is a lot of expertise residing in the Dow Chemical Co. on dioxin and what it is all about. They have been studying the effects of dioxin for over two decades.

To me, it would be extremely helpful if there was some way that we could involve their scientists, who are extremely able, in some kind of cooperative process, and avoid the confrontation and the unpleasantness of the past. It would be good to just get all the brains and the talent in Dow and in the EPA, perhaps, and a good medical school, working together using the data that Dow has accrued over more than several decades, to buttress an attempt to make some reasonably sound value judgments as to what the short-term, and middle-term, and long-term health effects are of dioxin.

I don't know that there is any repository of data around anywhere that would be as useful and helpful and as effective as the data that Dow Chemical Co. themselves have collected over the past several decades.

It just seems a shame that we have not been able to work out a joint study team or a joint task force approach of some kind that would start out with a Tabula Rasa, a clean slate, and wipe away some of the confrontation and the antagonisms of the past.

Dr. BARNES. Historically there is a precedent to that. We in the mid-70's had taken litigation to remove the registration of 2,4,5-T. One of the problems that we ran into at that time was that we when we went into the litigation, we found that we could not demonstrate that there any dioxin in the environment. We did not have any method capable of detecting this at that very low level.

We went from being adversaries to working jointly on developing an analytical method to develop the capability to detect dioxin in the low parts per trillion range.

It is that methodology that has given us the kind of data that we are generating now. It is precedent for the fact that we can essentially move ahead. I would like to see that day come again.

Mr. SCHEUER. I think we all would, yes.

Dr. MILLER. Mr. Chairman, I am sure you realize that we at FDA have had considerable expertise in this area. Very often the data that you need in order to determine a proper regulatory stance is somewhere in the files or the bowels of some company's records.

Through the years it has been very difficult to get that data out, largely because companies generally feel that by being identified with it is a liability question, et cetera, et cetera, that they have to face.

Our experience has been that when we work through responsible trade associations, particularly the more technically oriented trade associations, that gets buried. The individual responsibility of the company is lost.

Meanwhile our own options in taking regulatory action at some later point, if appropriate, are maintained. But the data comes to us, and we have the data and we need to operate.

It seems to me that in this issue there are organizations like the Chemical Industries Institute of Technology which have a fine reputation for good work, that could act as a clearinghouse for this information from the industry for this purpose.

Mr. SCHEUER. Can you give any specific recommendations on a research program design that you might recommend to bring us to the point where we could make some regulatory control judgments about dioxin? Would it be possible to work through the chemical manufacturer's association.

Dr. MILLER. I think there have been a lot of different research areas that have been outlined through the course of these hearings so far. I think in written testimony, particularly, there has been quite a bit.

From a regulatory point of view, it seems to me that there are really three things that we need to know. One is this fundamental issue of the sensitivity of man to TCDD. It is just absolutely essential to make some kind of rational regulatory action to know in fact what the hazard is to human beings.

Second, we need to know the distribution of dioxin in the environment. We are collecting that. In our case in particular it is the Food and Drug Administration that is collecting that data. We need to know also what the possibility is that food products can become contaminated with TCDD under various circumstances.

Mr. SCHEUER. And the possibility of what?

Dr. MILLER. The possibility that foods could become contaminated. Right now our evidence suggests that it is only fish. But is it possible that other foods because of other activities could in fact become contaminated as well.

And the third thing is the method of analytical methodology which is keyed to taking any kind of action. The last two are being covered, I think, in most of the research areas. It is the first one in particular that I think has to get a deal of attention.

That is going to require, based on the question of human sensitivity, closely coordinated research between all of the agencies, and

as you say, industrial organizations and universities that are involved in this area.

I suspect that what we are going to need somewhere along the line is some kind of steering group. I am not a firm believer in proliferating steering committees. As a scientist I like to be left alone to do my work.

I think this is one of those issues where we are going to have to have some kind of way of making certain that directions are being maintained and interactions between groups are being maintained.

Now here is, I think, an opportunity for not only the Government agencies to be involved, but also, for example, veterans groups that have an interest, VA, et cetera, and the industries, who, I think, have an important role to play in this. In that way this kind of thing can be coordinated in a reasonable way.

Mr. SCHEUER. Dr. Barnes, can you tell us what specific role did the EPA's chlorinated dioxin work group, and the chlorinated dioxin task force play in developing an action level for dioxin in soil of one part per billion, and in determining the Agency's response to dioxin contamination found in Missouri and in some other parts of the country?

Dr. BARNES. Both the chlorinated dioxin's work group and the chlorinated dioxin task force are entities within the Agency that receive dioxin problems associated with disposal sites and contamination. The group received information about a number of sites from the State of Missouri along with a request from our regional office for some sort of guidances about what should we do about these levels.

The dioxin task force and the chlorinated dioxin's work group reviewed that information and came up with a series of recommendations to the region. The Center for Disease Control was also asked by our regional office to come up with certain recommendations.

The Center for Disease Control generated specific guidance related to a number at least in one area. The Center for Disease Control generated a number. Our guidance was more general.

What we did was to lay out the spectrum of risks that I mentioned before, of risks versus concentration in the soil. We presented that to the decisionmakers and said, you know, you can pick off of here at any point given other nonrisk factors in order to make the risk management decision.

We went through an analysis and presented that to the decisionmakers. The number they came up with, at least in the Time Beach's area, was the one that CDC was espousing at the time, or the one part per billion.

Mr. SCHEUER. Were there any attempts by any EPA officials to influence or subvert the role and the recommendations of the dioxin work group?

Dr. BARNES. There was some concern raised within the Agency that that might be the case.

Mr. SCHEUER. I am not talking about what might have been the case.

Dr. BARNES. Right.

Mr. SCHEUER. I am talking about what was the case.

Dr. BARNES. My impression was that there was not. That impression was a misimpression. There were no attempts to subvert the role of the chlorinated dioxin's work group.

Mr. SCHEUER. I have a memo here dated September 17, 1982, from Edward Kurent, Acting Associate Enforcement Counsel, to Michael Brown, Acting Enforcement Counsel.

He says:

> Dealing with the potential problem in process and potential outcome of determination of cleanup levels for dioxin in soil, the purpose of this memorandum is to inform you of several potential problems which may be developing in Rita Lavelle's Office.
>
> These problems concern the process and end result of determinations of action levels for 2,3,7,8-tetrachlorodibenzo-p-dioxin, popularly known as TCDD or dioxin.

A little further down he says:

> The potential of the problem is as follows. As a result of an investigation by region VII, soils have been found containing detectable levels of TCDD, including some soils in home areas and people's back yards.
>
> Both for enforcement purposes and possibly Superfund purposes, an action level and proposed remedy must be developed.

Normally such decisions are made by the chlorinated dioxin work group and the chlorinated dioxin task force.

I am informed, however, that Dr. Arthur Palotta, Rita Lavelle's personal science adviser—he is a private consultant working directly for Rita—has injected himself into the decisionmaking process in a rather forceful way. He has performed a so called exposure/risk assessment that he claims indicated that exposure to 100 parts per billion of dioxin in the soil would be acceptable, that is, no remedy is necessary below this level, et cetera, et cetera.

My staff has discussed the situation with the Superfund Office and believe that they are strongly leaning toward requiring removal of all soil at or above one part per billion, covering the remaining soil and requiring the usual notice, et cetera.

The Superfund people and the Office of Waste Programs Enforcement and my Office are concerned, however, that because Dr. Palotta is aggressive and seems to have Rita's ear that he may get the chlorinated dioxin work group's recommendation reversed. He has been extremely adamant and vocal in meetings. Because the Superfund Office and the Office of Waste Programs Enforcement work for Rita, they are reluctant to take on Dr. Palotta.

Would you care to comment on this matter?

Dr. BARNES. Yes. I am familiar with this memo.

Mr. SCHEUER. Would you like a copy of this memo?

Dr. BARNES. I've got it.

Mr. SCHEUER. You've got it.

Dr. BARNES. I am familiar with it.

Mr. SCHEUER. OK.

Dr. BARNES. Dr. Palotta is a forceful individual. He has a forceful personality. But, at least as far as I was personally concerned, I did not find that overbearing or having an inordinate impact.

I know that some people felt as though he was perhaps a little aggressive. That is just his nature. I took it to be such.

When the chlorinated dioxin's work group and the chlorinated dioxin task force addressed these issues, on occasion Dr. Palotta would come. I remember one occasion where I was making a pres-

entation of laying out these risks. I presented a graphical analysis. Dr. Palotta felt as though he was in strong agreement with that general approach.

Then the question would come up, you know, at what level should action be taken? In other words, it is a risk management decision. That was a decision which gets into the risk management area. That was left up to the Assistant Administrator for Solid Wastes and Emergency Response.

But we made out presentation to Ms. Lavelle with many other people present. We laid out that spectrum of risks, and as far as I know, at that meeting no decision was made. Now what factors went into Ms. Lavelle making her decision about one part per billion, I don't know.

I know there were some people who were saying that one part per billion was too low. That in some areas 100 parts per billion might be more reasonable. As I said in my testimony, the one part per billion is not a universally applicable number. It is a number where you are concerned about children possibly access to this.

I could conceive of situations where somebody might say 100 parts per billion is not a level of concern. As a matter of fact, there is Agency precedent that I think antedate's Ms. Lavelle's even, where that decision was made.

We had originally told a company that we felt as though you ought to dig up some wastes and clean up everything down to non-detectable levels.

They cleaned up all the drums and all the liquids that were there. They kept digging and analyzing the soil, and they kept finding it. Finally, when they were many feet under the ground, they said, look, we still have hundreds of parts per billion of this stuff left.

Can we stop?

The judgment was made then that it was material that was well below the surface. It was in the back of somebody's farm. It was very unlikely that the dioxin was going to move from that area. It was very unlikely that exposure would take place. Consequently, the decision was made that in that case hundreds of parts per billion did not represent an unreasonable risk.

Mr. SCHEUER. Congresswoman Schneider.

Mrs. SCHNEIDER. Dr. Miller, I would like to ask you a couple of questions as it relates to your experiments and testing with fish.

If you have already set a standard for fish at the 50 parts per trillion level, why are some States going ahead and establishing fish numbers on their own?

Dr. MILLER. In the first place what we established was a level which we call the level of concern. It has no legal standard.

Mrs. SCHNEIDER. I understand.

Dr. MILLER. It actually was designed to provide advice to the States in exactly that area.

Second, the fundamental issue is that the nature of the exposure to dioxins, that is the TCDD, is such that every area has to determine what that exposure is, and from that determine what the acceptable level of exposure is.

It depends on how much fish people eat, how much fish in the fishery is contaminated, and which fish are contaminated. This will vary from place to place.

I think the third point that needs to made is that our recommendation of a level of concern was really 25 parts per trillion. Below 25 parts per trillion we said that we thought it was safe. Above 25 parts per trillion we said now limit the amount of fish you eat.

From our regulatory point of view, we cannot do that. We cannot establish a national standard with a proviso, so to speak. It either is or it is not.

Mrs. SCHNEIDER. These are just guidelines for the rest of the States.

Dr. MILLER. These are guidelines for the States. Exactly. We work closely with most of the States in the contaminated areas to keep an eye on this and to determine what the possible risks might be.

Mrs. SCHNEIDER. One factor that rarely is discussed is the accumulative levels of dioxin or other types of pollutants in the human body.

Is there a transfer from the soil to the crops of TCDD?

Dr. MILLER. There has been, I think, several experiments done attempting to determine if any TCDD is actually transferred, particularly into root crops of one kind or another. The answer is thus far no one has been able to determine that that occurs. That there is no transfer into root crops.

We have some data on rice grown in areas in Louisiana that have been sprayed with things like 2,4,5-T and so on, and we found no dioxins in the rice. We found no TCDD or any other dioxins for that matter in the rice.

As far as accumulation of dioxins in humans is concerned, a lot of that depends on the availability of the dioxins. The TCDD is present in soil. Its availability may be different than the TCDD that is found in fish flesh, et cetera. It varies a lot.

A final point is that our risk assessments were based upon the assumption that people are going to be exposed to these higher levels throughout their life. So that issue of accumulation then, was in fact taken into account as we made our risk assessments. We simply assumed the maximum kind of exposure as we did them.

Mrs. SCHNEIDER. In addition to the accumulation one also has to take into consideration the synergistic interactions of TCDD and other types of pollutants which might ignite cancer or other health problems.

Obviously, what we are dealing with is enormously complex, and I would think that the FDA would not want to be putting itself in a position where they are underestimating or attempting to underrate the amount of exposure that would be acceptable given the fact that this is one little element in one little source of health concern.

Dr. MILLER. That is quite true. The interaction among environmental food-borne contaminants is a very complicated affair. No one really knows quite how to deal with it.

In fact, to show you how complicated it is, in some cases two substances which are of themselves toxic, will in fact be antagonistic to each other or reduce the toxicity to each other.

Nevertheless, our assumption from the beginning is that these are effects that insist on us taking the most conservative estimates that we can, within reason. The Academy, I think, said there were 34 different items that had to be considered in a risk assessment. If you add conservatism upon conservatism pretty soon everything is unsafe. You don't have to worry about getting cancer because you will starve to death.

Along the way somewhere you have got to put some limits. In our case, and as with our colleagues at EPA, generally speaking we have been criticized because we have been too conservative. But I think we have to be.

Mrs. SCHNEIDER. Are you familiar with dioxin problems in other countries outside the United States? For example, where?

Dr. MILLER. The only place that has admitted thus far to the finding of TCDD in their food supply of any kind has been the Canadians. Of course we have worked very closely with them.

In addition, we have worked closely with our colleagues in the United Kingdom through a treaty agreement called the Tripartite Agreement. Their results have given us some idea of what the extent of contamination might be, not only in the United Kingdom, but in the Common Market countries.

It is, I believe, a worldwide problem. Not in the sense of the kind of thing we find in the Tittibawassi River or in the Love Canal situation. But the fact is that I think we will find TCDD's are very widely distributed in the environment.

One of the problems we are simply going to have resolve is what is this background level to which we have always been exposed to, compared to these peaks.

Mrs. SCHNEIDER. Right.

For example, how are the Canadians dealing with their dioxin problem? Do you have some data on that?

Dr. MILLER. As I said, we and the Canadians have been working very closely. We have established, in our case, levels of concern, and in their case, action levels because of the different laws under which they operate, that are virtually the same.

I think they have set it at 20 parts per trillion, and ours is 25 parts per trillion, which is basically the same.

We have been meeting informally almost continuously on this and other such problems. But we are meeting much more formally with them in September, along with our colleagues from EPA and the United Kingdom, on exactly this issue.

We exchange data all the time. They have, for example, data on a wide variety of foods. They have data on beef and pork, on eggs, and on milk. We have some data on, as I said, crawfish and other crops.

On everything but the fish, out of those areas where there are these spike contaminations, we don't find any TCDD above the level of about 10 parts per trillion.

Mrs. SCHNEIDER. Are we most advanced insofar as determining the levels of pollutant in the fish area?

Dr. MILLER. I would say that we and the Canadians are probably leading in this respect. We have probably put the most effort into this.

The Bureau of Foods has invested a substantial portion of its chemical contaminants program money into this area of dioxin. The health protection branch's foods director has done a similar thing.

Our scientists are constantly exchanging information.

Mrs. SCHNEIDER. Good.

Dr. Barnes, I wonder if you could just outline for me briefly what the EPA task force on dioxin strategy is going to be?

Dr. BARNES. What it's going to be?

Mrs. SCHNEIDER. Yes.

Dr. BARNES. Basically, this is a group that has recently been formed under the auspices of the Office of the Deputy Administrator. They are trying to come up with a strategy of how to deal with the dioxin issues that are arising in the country today.

The task force has been named. A draft document has been prepared. It has been the subject of discussion at a meeting with all of the regional administrators present.

The comments are now coming back in from the region on that document. Within the next couple of weeks, as I understand it, a document will be prepared from the Deputy's Office and submitted to the Administrator's Office for his review.

The thrust of it is sort of in line with trying to deal with largest problems that we see first. We see the largest problems being associated with the sites of previous manufacture of certain chemicals which had 2,3,7,8-TCDD as contaminants.

If you look around the country and you say where are the dioxin problems, at nearly every site you can identify it or link it to, let's put it that way, if you cannot establish a direct cause-effect relationship, you can link it to the previous manufacturing of chemicals that contain 2,3,7,8-TCDD. At the current stage that would be the thrust of it.

In addition, there would be considerations of additional research that needs to be done which we have already discussed today. Some of the areas that we think need to be highlighted are as Dr. Miller has suggested, this question of the mechanism of action that I discussed earlier in the day. I think that is critically important in the mid to long term.

In the short term I think that is most important is the question of bioavailability, where we find it in the environment as different from buying it from a chemical company and feeding it to a rat. You have to say what is the toxicity as it exhibits itself in the environment.

Again just to follow up on another of special interest to EPA is the question of disposal and destruction. As we go to these sites and we identify areas, the question then is what do you do about that situation.

First of all you must answer the "so what" question. Just to go out and generate numbers to say there is so much dioxin present does not really do much to help the public health. As a matter of fact it may just raise certain anxieties.

You have to have procedures in place to say what you are going to do about it. This comes back, in most cases, to limiting exposure to this material, either by removing the people or putting in some sort of barrier. This latter case is probably going to be followed in the future.

Mrs. SCHNEIDER. Thank you for that very specific answer.

To what degree are you interacting with the other four Federal agencies that are also doing dioxin research?

Dr. BARNES. We are joint members with them on the agent orange work group. We meet with them monthly.

In addition, we are represented on the science panel, which is the subgroup of that group, which is charged with coordinating Federal research on dioxin activities.

From the HHS chaired agent orange work group there is a whole layout of the research that is presently being conducted by the Federal Government in the dioxin area, which added up goes to tens of millions of dollars or even more than that. We participate with them on a continuing basis.

Mrs. SCHNEIDER. OK. Thank you very much.

Thank you, Mr. Chairman.

Mr. SCHEUER. Dr. Barnes, when you were describing this little collaborate effort between EPA and Dow——

Dr. BARNES. Yes.

Mr. SCHEUER [continuing]. To do a joint study of the discharges from the Midland plant into the Tittibawassi River, I didn't get clear in my mind whether EPA was going to have access to the raw data, whether they would be able to measure it there, or whether Dow was going to pass on the digested and analyzed information to EPA.

Can you clarify?

Dr. BARNES. I am not sure that I can at this time. As I indicated there is going to be a meeting to discuss those kinds of issues and others in August. As I understand the instructions from the subcommittee that anything formal that comes out of those kinds of meetings we would communicate to the subcommittee.

Mr. SCHEUER. Yes.

I would strongly urge that in such a meeting that it be arranged and agreed that EPA personnel be allowed access to the site, that they be involved in the measuring process, and that they be involved in the analytical process. This is so that they can speak for EPA in saying we have analyzed that discharge, we have measured it and we have analyzed it and this is our conclusion, and it jives with the conclusion of the Dow experts.

Dr. BARNES. As an example of that kind of activity, within in the past year we have worked with Dow Chemical Co. on this question of bioavailability.

We did the joint study with them of exposing fish to dioxin contaminated material. EPA did the exposure and then we subdivided the fish. Some went to Dow and some went to EPA. We analyzed and checked each other's results.

In those cases we agreed very much with what they obtained. So I think that's precedent again to indicate that that would be a fruitful kind of activity.

Mr. SCHEUER. I would be unhappy and disappointed, too, if I were to hear, after all the dust had settled and the smoke had cleared, that the EPA people never had first hand access to the plant, and never had their people studying the discharges themselves, and were not in on the evaluation process. It seems to me they have got to be in on the takeoff as well as the crash landing.

Dr. BARNES. I understand.

Mr. SCHEUER. This is necessary for those of us in the Congress to have a feeling of confidence that this was a truly joint effort and it represented the best thinking of both the excellent scientists at Dow as well as the excellent scientists at EPA.

Now you have over at EPA authority to regulate dioxin under the Clean Air Act, under TSCA, and under the Clean Water Act. Right? EPA has this authority under three different pieces of major legislation?

Dr. BARNES. Yes.

Mr. SCHEUER. Now what activities are going on at EPA to regulate dioxin under any or all of these three pieces of legislation?

Dr. BARNES. Under the Clean Air Act the concern there would be what kind of ambience standards or area mission standards that ought to be established.

To establish an ambient air standard or any kind of a standard is a very long process. The first steps to investigate the possibility of that are being taken right now.

We are finishing up a literature search on published data of dioxin levels in the air. We are trying to determine the extent to which this is a problem.

We have found dioxin from certain combustion sources. But in our risk assessment analysis to date, we have not found them to have a significant health impact. We are looking beyond our own data to the world's literature. Within the next month or so we expect that literature search to be completed. An analysis of that will be made as to what the next steps ought to be concerning dioxin in air.

Concerning the water, we have authority to come up with criteria as to what we think would be reasonable levels of dioxin in the water. At the end of this month, in 2 weeks, there is going to be a meeting in Cincinnati where reviewers from around the world literally, will be coming in to look at the assessment that we have made of dioxin in water.

As an outgrowth of that document we expect some suggestions being made as to what the appropriate level would be in the water.

At that same meeting in Cincinnati a significant document based upon the health effects of dioxin in the air will also be reviewed. Also at that meeting will be a document that we have prepared about dioxin from waste sites, which gets us to the resource conservation and recovery program.

Mr. SCHEUER. Now before you get that far, let me just break in to say that the baseline data for that study was done by Dow.

Dr. BARNES. That is correct.

Mr. SCHEUER. What was the underlying rationale for the Agency's activity in this connection, and the reason for using the Dow study as a baseline?

Dr. BARNES. What we are talking about here specifically——

Mr. SCHEUER. What was the degree to which EPA personnel may have participated in that study and knew of its authenticity and reliability, and could vouch for the integrity of the process from their own experience?

Dr. BARNES. OK.

What we are talking about explicitly are two studies which have been conducted by Dow Chemical, one in the area of cancer, and one in the area of reproductive affects.

These studies have been conducted and submitted to the Agency and independently presented to a peer review journal. It is now part of the world scientific literature. I think almost without exception these two studies are used by most risk assessment people in this country and abroad, at least to date, as the most definitive kinds of studies that have been done.

Our experience with the Dow scientists and the Dow science is very much as you have referred to earlier, that we have not found reason to think there is a problem.

As regards your question have we been a part and parcel of that experiment, we have not. I believe that raw data has been submitted to us as part of our activities in the litigation of 2,4,5-T. We have looked very stringently at those studies and the background documentation and the raw data themselves. I believe that I am correct in that. I can check and let you know specifically.

We, and I think other risk assessors, have fairly good confidence in those data. Now in terms of the interpretation of those data, we do not necessarily agree with Dow. Our risk assessments are somewhat different from theirs because we interpret the data somewhat differently. But the raw data are there for scientists to look at.

Mr. SCHEUER. Then you have no question about the authenticity of that baseline study and the raw data base?

Dr. BARNES. I have no reason to doubt the integrity of that material at all.

Mr. SCHEUER. All right.

We very much appreciate your patience with us. We plan to submit some written questions for the record. We thank you for having sat here for several hours until well after 4 p.m.

With that we will adjourn this meeting.

[Whereupon, at 4:10 p.m., the hearing was adjourned subject to the call of the Chair.]

DIOXIN—THE IMPACT ON HUMAN HEALTH

THURSDAY, JULY 28, 1983

HOUSE OF REPRESENTATIVES,
COMMITTEE ON SCIENCE AND TECHNOLOGY,
SUBCOMMITTEE ON NATURAL RESOURCES,
AGRICULTURE RESEARCH AND ENVIRONMENT,
Washington, D.C.

The subcommittee met, pursuant to call, at 9:45 a.m., in room 2318, Rayburn House Office Building, Hon. James H. Scheuer (chairman of the subcommittee) presiding.

Mr. SCHEUER. The subcommittee will come to order.

Today the subcommittee is continuing its hearings on dioxin and the likelihood that dioxin represents a real danger to public health, particularly public health in the workplace.

At our previous hearings on this matter, we have heard conflicting testimony regarding the short-term and the long-term adverse health effects to humans that stems from dioxin exposure. While it is true that many unanswered questions remain, I'm confident that as the record of these hearings is accumulated, it will become obvious that we have moved across an important threshold in our national debate about dioxin.

At a point not more than about 100 days ago, we were arguing with EPA and the major chemical companies about where dioxin contamination was occurring and whether or not it constituted a health hazard any more severe than smoke given off by char-broiling hamburgers.

What we have learned about dioxin should arouse deep concern among prudent people. We have heard testimony that dioxin, this useless toxic byproduct in the manufacture of widely used chemical herbicides, kills large and small laboratory animals.

The EPA has concluded that dioxin is the most toxic substance that they have ever tested and that it "probably"—I say that in quotes—causes cancer in humans. For the air, EPA now estimates that a trillionth of a gram of dioxin in a cubic foot of air can be expected to result in 9 additional cases of cancer for every 100,000 people in the population.

For water, EPA now suggests that it is unacceptable to have dioxin concentrations of more than 2.1 parts per quintillion. A quintillion is followed—is a 1 followed by 18 zeros and is equal to 1 billion billion. I am not sure that we are able to measure 2.1 parts per quintillion, and perhaps the scientists who testify will enlighten us.

This morning, we will be hearing about a dramatic study being undertaken by the National Institute for Occupational Safe and Healthy—and Health, hereinafter to be known as NIOSH.

As we move past the question of whether or not dioxin exists and whether it is harmful to humans, the NIOSH study becomes a highly sif. t milestone and should be a major guidepost to us as we contemplate the type of research and the type of regulatory and legislative activities that should be the focus of attention of policymakers, both on the executive branch and in the legislative branch, concerned with protecting the health and the lives of the American public.

The irony of the NIOSH study is that it takes previously known pieces of the puzzle from widely scattered small samples and assembles these statistics in a holistic coherent fashion that allows us to assess more adequately the full scope of the dioxin problem.

The small pieces have been evaluated in a fashion to deny that a problem has existed. Now all of the pieces fit into a larger whole that demonstrate convincingly that the problem exists and is growing.

A chemical byproduct like dioxin that kills animals, harms marine habitats, and may cause fatal cancer in humans is a very serious byproduct indeed.

We are very pleased this morning to have a distinguished group of witnesses. The seriousness with which the administration is now treating our concerns about dioxin is underscored by the requests we received in the last day or two from Dr. Edward Brandt, the Assistant Secretary for Health, to appear and testify this morning. We welcome Brandt back before our committee and we look forward to his comments.

Dr. Irving Selikoff, one of the Nation's leading environmental health authorities, and Dr. Philip Landrigan, who has led the NIOSH study, will be sharing with us some of the details of the study and the wider implications that we must consider in coping with this potential health hazard.

We also will be hearing this morning from members of a national veterans' organization vitally concerned with the health damage that may have been done to American soldiers as the result of dioxin exposure in Vietnam.

Maj. Gen. Murphy Chesney, Deputy Surgeon General of the Air Force, will also discuss the recent and controversial study conducted by the Air Force on personnel with limited exposure to agent orange defoliants, which of course, contained the toxic element, dioxin.

Ultimately, we in Congress are faced with the question of how much we know, how much we ought to know that we don't know now, and what we should be doing about it now and in the future. One answer is that we know a great deal and none of it is very comforting. We hope this morning to make a start down the road of what we know—of defining what we know, of defining the kind of research we ought to do to accrue the additional knowledge we need to know to legislate and regulate more precisely.

Ideally, this should be done in a cooperative relationship among Congress, the executive branch and the chemical companies. We know there is an enormous amount of talent out there in the pri-

vate sector: brilliance, professionalism, and decades of knowledge about these chemicals. And we hope very much that they will be harnessed in some kind of a collective effort to find the answers to the questions that will be posed this morning and that we have been wrestling with.

The American people will certainly wrestle—will certainly welcome such cooperation. The time for confrontation really should have—should be behind us; the time for cooperative efforts to solve the problems that we now see emerging is here upon us.

Should one or more of the proposed partners in this relationship, either for commercial or political reasons, choose to be obstructionist, I'm sure the American people will appreciate policymakers in government who put protecting the health of the American people ahead of protecting profits in the private sector.

Animal studies have shown dioxin to be among the most toxic material known to man and the results of dioxin studies on humans, as they are now emerging, will be the subject of our focus today and what they will tell us about the effects of dioxin on human health.

It is my hope that the uncertainties regarding the effects of humans exposed to dioxin can be resolved, based on the NIOSH study, the Air Force study, and further studies patterned on these.

Having said this, I would now like to turn to our very distinguished ranking minority member of the subcommittee, Congressman Ray McGrath of New York.

Mr. MCGRATH. Thank you, Mr. Chairman. I want to join you in welcoming our witnesses here today.

In previous hearings on this subject, we have heard testimony that one of the most serious difficulties scientists encounter in dioxin research results from the fact that dioxin exposure seems to affect each species differently. For this reason, it is difficult to extrapolate the results of animal research to human beings.

I'm very pleased this morning that we have before us witnesses who have experience in the study of dioxin effects on humans, health effects in humans. I look forward to their testimony and also to any guidance they can provide the subcommittee regarding the directions for future dioxin research. I would also point out that in today's testimony from our distinguished panel, we are going to hear, for the first time, at least in these hearings, evidence from studies from the Air Force and others that there is a causal relationship between dioxin and cancer. I refer to this morning's Washington Post where Dr. Philip Landrigan, the Chief of Surveillance Evaluation and Field Studies for NIOSH, is quoted as saying that "the evidence very strongly suggests that occupational exposure to dioxin can cause cancer."

Now, this is the first time that we on this subcommittee have heard language like that. We have heard language that seemingly said that, but never to that extent, and never that strongly.

So I'm delighted that the panels are here today. I want to welcome Dr. Selikoff from Mount Sinai—I have a little interest in Mount Sinai myself—and I am looking forward to the testimony of all of our witnesses.

Thank you, Mr. Chairman.

Mr. SCHEUER. All right. Well, Dr. Irving Selikoff, would you join us at the table? Dr. Irving Selikoff, director of the environmental sciences laboratory at the Mount Sinai School of Medicine.

We are delighted to have you, Dr. Selikoff. Your testimony will be printed in full in the record, such as it may be. What we would really like you to do is take whatever time you need and just chat with us and unburden yourself of your insights and your professional views about this whole matter.

STATEMENT OF DR. IRVING SELIKOFF, DIRECTOR, ENVIRONMENTAL SCIENCES LABORATORY, MOUNT SINAI SCHOOL OF MEDICINE

Dr. SELIKOFF. Thank you very much, Mr. Scheuer. Thank you, Mr. McGrath.

Mr. SCHEUER. Would you be kind enough—going off the record—to pull that mike a little bit closer to you so that we can——

Dr. SELIKOFF. I think maybe it would be even better to put it on.

Mr. SCHEUER. Yeah, that would help. Is it on?

The REPORTER. No. Push the lever forward.

Dr. SELIKOFF. Here? There it goes.

Mr. SCHEUER. Let's try it.

Dr. SELIKOFF. Thank you——

Mr. SCHEUER. That's fine.

Dr. SELIKOFF. In that case, I will again thank you, Mr. Scheuer, and Mr. McGrath, for having me here. I will speak as a scientist, and to the extent possible, I will tell you something of the way scientists feel about this problem, both from their point of view and from the point of view of their ultimate objective, that is, prevention of human disease.

Mr. SCHEUER. I take it you will discuss the NIOSH study?

Dr. SELIKOFF. Oh, I think with Dr. Landrigan here——

Mr. SCHEUER. Oh, you leave that to him.

Dr. SELIKOFF. I would allow him to do that because he will be able to do it extraordinarily well.

Mr. SCHEUER. Very good.

Dr. SELIKOFF. It is now more than 25 years that dioxin was identified as a hazardous contaminant of chemical manufacturing; 25 years as we sit here, 1957. This was soon confirmed in a series of industrial accidents and a large variety of animal tests to which you have referred.

We, therefore, have had ample warning that here was a virulent, toxic agent that had better be controlled. It is, therefore, disconcerting to find that it's broadcast throughout our country in toxic chemical waste sites and chemical plants in cities and villages and towns and herbicides and industrial products, in rivers and fields.

Equally frustrating is recognition of the scientific incompleteness and inadequacy that exists. Indeed, the fact that this hearing is being held and your introductory remarks give point to that.

We've studied a good deal. The EPA, for example, has done a superb job in detecting, analyzing, tracing, and measuring this chemical. In fact, you brought me an order of magnitude lower in our ability to concern—ability of detecting dioxin in concentrations now, and perhaps a year from now we will be able to do even an order of magnitude better than that.

Mr. SCHEUER. Excuse me, can we measure 2.1 quintillions——

Dr. SELIKOFF. Sure.

Mr. SCHEUER. We can.

Dr. SELIKOFF. And we will be able to do better. There are some chemicals now that we can measure in number of molecules, in 10, 20, 50 molecules.

Mr. SCHEUER. Per what?

Dr. SELIKOFF. Per sample that is given to us. The analysts are excellent and they are getting better and better and their equipment is also being better and better utilized.

However, we have very little or no knowledge of what to expect as a result of the contamination of public water supplies, for example. I think it was just 2 days ago that the New York Times had a long article on the fact that about one-third of the American public is now drinking water—primarily ground water—that is chemically contaminated and I guess in a very abashed way, the statement was made that we don't know what the health effects are going to be, that one-third of the American people could be drinking water with chemical contaminants and we don't have the vaguest idea at this time what the potential health effects are going to be. That is very disconcerting.

Physicians have literally no idea of what to look to for early diagnosis of people who have perhaps been exposed, which cancers or other diseases are going to occur. Dr. Landrigan's group has done an excellent job in bringing together the information on soft tissue sarcomas, but we have no way of knowing whether these are the cancers of interest. What he has been able to do—very important it is, indeed—was to demonstrate that this chemical can cause human cancer. Which cancers are still far beyond us.

It reminds me of the 1950's when we knew that cigarette smoking was likely to cause cancer, but we had no idea of what the ultimate spectrum was going to be. For example, cigarette smoking increases the risk of cancer of the tongue. That is a very rare disease. In our whole country, there would only be a small number each year. If we did studies that showed that cigarette smoking increased cancer of the tongue—well, I don't think that would have led to congressional action on warning for cigarette smoking. Rather, the subsequent studies showing that it also vastly increased the risk of lung cancer, that led to the problems that we now face, because instead of a handful of cancers of the tongue that we would have identified, we now expect this year to have over 115,000 deaths of cancer of the lung in our country—still a majority in males, although women are rapidly catching up to us. They've come a long way, baby.

Now, municipal and State authorities—and it is hardly a week that goes by that we're not called by one or another municipal or State group—when dioxin is found, don't know whether they should react as a disaster or whether this would require a simple contamination cleanup.

Now, you've mentioned the animal studies that have been done, and they've been very well done, particularly in the 1970's. How do we interpret these? There is a significant difference among the various species: Hamsters are resistant; dogs are resistant; guinea pigs

almost fall over at the sight of a molecule of dioxin. Where do humans fit in?

The ability to translate the animal studies to evaluation of human disease has not been addressed and so we have a large number of very good, very accurate animal studies. Their significance in terms of what is going to happen to Americans is not known.

Do the animal studies, for example, predict that dioxin is going to add to our country's cancer burden, which now takes one out of every five Americans, one—20 percent of all Americans now die of cancer. Is this going to be added to, not simply by soft tissue sarcomas or Hodgkin's disease, but by a whole variety of other cancers that may occur?

When animal studies show misshapen pups and rodents, does this mean that we are going to augment the 4 percent of all births in our country that now end in birth defects? We can't answer that question at this time.

Are we to expect, as Dr. Landrigan now tells us, soft tissue sarcomas, or are we going to have, let's say, a 50 percent or small increase in lung cancer or pancreas cancer? We can't answer that question.

Do dioxins in, let's say, waste sites, chemical waste disposal sites, interact with other chemicals that are there, because these sites don't contain only dioxin; they contain a whole variety of toxic and carcinogenic chemicals.

We have no idea of what the interaction products are or what multiple exposures may be. Two days ago, the Wall Street Journal carried a story about the EPA field inspectors now going into the waste sites in space suits—and I think that is perfectly justified, they are absolutely accurate—but if you went there the day before or a day later, you would see members of the operating engineers' union in their bulldozers pushing this stuff around. No, they're not in waste suits; they're in teeshirts and nobody has warned them about the dangers of walking through these toxic waste sites. No one has even told them whether or not they should change their work clothes before going home.

I think it was today's Post to which you referred that told us that the son of one of the chemical plantworkers who had soft tissue sarcoma also developed soft tissue sarcoma and died. This is, of course, reminiscent of what happens when beryllium is brought home by workers on their work clothes, with beryllium disease then found in the families, or what happens when an asbestos worker brings the dust home to his family with subsequently cancer seen in the wives and children.

Doctors at this time, for example, just can't answer such simple questions as are patients with kidney disease or liver disease or heart disease or blood disease more susceptable than others? They can't answer a simple question from—let us say the proverbial Mrs. Smith—is it all right for my 5-year-old daughter to drink this water? They can't at this moment answer that question.

Some weeks ago, one of my colleagues, and an organization to which I belong, the AMA, ah, was clearly very exasperated. It was a Missouri physician and he introduced a resolution at the AMA

convention expressing his exasperation and frustration, a resolution on dioxin which was passed by the convention.

I've heard criticism of this, that it was intemperate, and that it was exaggerated. I submit, however, that it was an understandable frustration and an understandable exasperation.

I would point out that scientists feel very much the same when they are asked questions like: Which cancers should we keep an eye out for? I don't know. Should people with liver disease or neurological problems be especially careful? We don't know. Should a pregnant woman be considered to have a special risk? Should she be drinking bottled water? We don't know. Should steamfitters and electricians and insulators and plumbers working in these plants where dioxin can be a contaminant, should they take special precautions? Should their physicians be told of their potential exposure and what might be expected?

We can't even tell veterans, for example—although I hope that eventually we will be able to—what special medical problems they might have. The—you will hear, I am sure, of the Ranch Hand study that is being done by the Air Force. I am very concerned about the fact that an unknown number of Vietnam veterans were not exposed in the Ranch Hand work, but rather with the very large amount—an unknown amount of agent orange that was applied other than by aerial spraying. It was applied by backpacks, for example. No one knows about the exposure that would have been suffered by a veteran who was applying agent orange around a parameter of a military site with a backpack. No one knows what the exposures would have been to Vietnam veterans staying at these sites for weeks and months. The dioxin stayed there, also, and as you know, it's—uh, to be found there for days, weeks, months, years, and exposures would have continued.

Now, the Missouri doctor to whom I referred had a right, then, to be exasperated. He, uh, was aware of numerous questions and very few answers. Answers that were not available because the essential questions have never been addressed.

There's been 25 years of research that hasn't been done; work is not examined; birth defects not sought; human cancer unstudied; the large studies needed to provide information on human health effects have been omitted. The Missouri doctor had a right to be frustrated. He might have considered, for example, that the soft tissue sarcoma signal—because that's what it is—it was a signal, just the way angiosarcoma of the liver was a signal that vinylchloride was a carcinogen or mesothelium, an otherwise very rare disease, was a signal that asbestos exposure was taking place, cancer could result. That this signal was first told us by a Swedish physician, Lennart Hardell, rather than our excellent scientists. He might have considered, for example, that the EPA today—there is a meeting in Cincinnati today of the EPA to consider its dioxin statements, very, very well done statements. I've reviewed them.

In that review, I found that EPA will present virtually no human data and that is—here we are now, at the end of July 1983. I have been accustomed to this. In 1976, when the tragic accident occurred in Seveso in Italy, when the Icmesa plant unfortunately had this explosion and square miles of the region around that plant were contaminated with dioxin, our Government wanted to do ev-

erything it could to help the Italian authorities in this tragic event and with the good offices of our State Department, the National Academy of Sciences convened a small group of scientists to explore our experiences and decide what we could advise the Italian authorities.

And among the scientists who were there were two from a very large chemical company which, more than a decade before, had had a dioxin accident in their manufacture of 2,4,5-T. We were shown pictures of the skin lesions of the workers at that time; they had a good deal of chloracne, and the accident was described to us.

When the scientists were finished, we asked a very natural question: What happened to these workers, and one of the chemical company scientists looked at the other, and the other looked at him, and it had never entered their mind to follow these people to see what happened over the long term, and we still don't know.

So that this—I have a feeling of deja vu with this situation now. The Missouri physician might indeed not only have been frustrated, but also quite pessimistic. This is a situation you're addressing that is becoming all too common: the widening gap between scientific concerns and our country's utilization of the scientific leads that are becoming available.

The situation that he might have addressed, I think, could perhaps be summarized by saying that we've had very few villians; I don't consider that the chemical companies have been villians; there have been certainly very few saints; scientists haven't had much of a chance to be saintly, but there are potentially only many victims.

Thank you.

Mr. SCHEUER. Thank you very, very much, Dr. Selikoff.

Let me state that we've been joined by Congressman Tom Harkin of Iowa and Congressman Harold Volkmer of Missouri and Congressman Tom Ridge of Pennsylvania, who is not a member of this subcommittee, but who is a Vietnam veteran and who has been attending these hearings very assiduously and very devotedly and we are looking forward to his comments and questions. We hope you will participate, Tom.

Dr. Selikoff, let me ask you a sort of summary question to start off with, sort of taking—reversing things. If you were sitting either in our shoes up here or in Dr. Brandt's shoes, who is making policy for the Department of Health and Human Services, if you were making health policy for the Congress and/or the executive branch, what kind of medical research do you think ought to be done to answer the questions that you think ought to be addressed to answer the unresolved questions that we ought to have answers to know about the health—the threats to human health of dioxin in terms of tell us what research we ought to do that would help us decide, first, whether dioxin is a matter of threat to the human health in the work place or is it far more than that?

Is it something that affects these 5,000 or 6,000 workers who have had intense and prolonged exposure to that dioxin, handling it over a period of a decade or two, or does it affect the whole length and breadth of Americans who are living at or near the dioxin plants where dioxin is being used to manufacture herbi-

cides—a dozen, perhaps 10 or 12 of those plants—or people who live near toxic dump sites?

What are the questions that you would want to research to address if you were making health policy? What kind of answers would you want to come up with in order to regulate the production of dioxin and the whole awesome business of cleaning up these tens of thousands of toxic dump sites around the country?

Dr. SELIKOFF. Can I go back to the late 1940's?

Mr. SCHEUER. Take us by the hand as far back in history as you care to.

Dr. SELIKOFF. Those of us here with hair like mine will remember the Smythe report—remember Professor Smythe of Princeton—who, after World War II, wrote a report on how we produced the atomic bomb. And in it, he pointed out that we knew that we had to isolate the important fractions of uranium, the important isomers, in order to produce the atomic bomb.

He said there were—it was clear to the scientists there were three ways of doing it: You could do it by ultracentrifuging, you could do it by diffusion, gaseous diffusion; you could do it by chemical separation in order to get out the—the chemical that you wanted.

In the ordinary—ordinary course events scientists would have taken the most logical, the most promising of the approaches, tried that, if it didn't work after 2, 3, 4, 5 years, well, you go to the next method, and if that didn't work, you'd go to the next method. But it was so important, they felt, that they decided to do all three at one time. And that's what I would do with dioxin. I don't think there is a single piece of research that should be done because it's most important, but rather, we would do well to utilize all of the scientific approaches that have promise at this time.

Now, in that, one thing that we would do—and here we have excellent capacity in the National Institutes of Health—we should learn how to translate animal studies to man. We don't at this point. We can't even translate from rat to mouse, much less from mouse to man.

This is by no means beyond us; there is a coherence in biology which indicates that the observations in one species have some means for other species as well, so that that basic research has to be done.

Second, the human health studies should take advantage of what we've learned in these 20 years. We know how to define and to develop information concerning human health effects. Cohort studies, for example, in which large groups of people are followed prospectively have given us the critical information that we have gotten for many of the agents that we now know are toxic to human beings.

In these, we take, generally, those most heavily exposed; see what happened to them, because that at least tells us which diseases are going to occur, and if you know which diseases are going to occur, that's almost half the battle.

Mr. SCHEUER. Do we perceive—should we perceive of dioxin in terms of its health effects on humans, to be a problem for the work-place or a problem for the general environment?

Dr. SELIKOFF. At one time, I would have answered to the workplace, but we've gotten burnt so many times now that we realize that a wire fence doesn't stop a product in the workplace; wherever you have a toxic agent, it sooner or later has a potential threat for the entire community. In fact, when in 1974, it was considered that we had better see what vinyl choloride is going to do—if you will remember, the cancers of the liver, the angiosarcomas of the liver in Louisville at the B. F. Goodrich plant. The second thing that was done after looking at the various vinyl chloride plants in Midland, Mich., and Niagara Falls, N.Y., and in South Charleston, W. Va., et cetera, was to see where else it was being used and the first place that we looked was the hair sprays that women were using with vinyl chloride as a propellant in little bathrooms, and when you measured the vinyl chloride concentrations there, they were almost as high as some of the factories.

So that we have learned that that can't be done. But this is particularly true with dioxin. If it contaminates herbicides, then it is going to be wherever herbicides are used. If it contaminates waste, it is going to be in every waste disposal site. If it is produced by high heat, with certain other halogenated aromatic hydrocarbons, it is going to be wherever high heat hits those substances.

If a transformer goes up in a fire and there have been chlorophenyls in the transformer, then firemen are going to be exposed to dioxin, so that it is—goes beyond only the workplace. But in the work place we can learn a great deal.

For example, I've mentioned the operating engineers using the bulldozer, the front-end loaders, et cetera, at the waste disposal sites. If they had no problem, I would worry very much less about a person living six blocks away. If, on the other hand, operating engineers do have various diseases, do have adverse experience, we at least know what to look for as things go on.

We don't know the danger of driving over roads along which dioxin-containing oils have been placed, but we know of thousands of teamsters, thousands of truckdrivers who have parked their cars for decades in parking lots that were covered with such dioxin-containing oils.

We know of—in New Jersey, for example, we have recently been concerned in Newark with the Diamond Alkali Plant, which closed in 1969. That plant, since 1969, has had numerous steamfitters, construction workers doing repairs, doing remodeling and so forth. The building trades unions in New Jersey have asked Governor Kane to have their people examined. They have already seen—they suspect—serious disease among their workers who have been employed in these chemical plants.

Maintenance workers throughout our chemical and petrochemical industry may be of concern in this regard, so that we know very well how to do it, but these studies have just simply not been done. I can't tell you why, for example, operating engineers have never been studied.

Mr. SCHEUER. Congressman Ray McGrath of New York.

Mr. MCGRATH. Thank you, Mr. Chairman, and thank you, Dr. Selikoff, for the enlightened testimony.

I sensed throughout your testimony, and even throughout the answers that you've given to the chairman, a sense of frustration, of

not knowing, not being able to extrapolate millions of dollars worth of research on animals from—as you say—from a rat to mice, or from animal to human, and certainly that is a frustration which we share here sitting on this side of the desk.

I often wonder what good all of these studies are if the scientists themselves and the regulatory agencies are not willing to stand behind their own research to the extent that they would not offer a standard of a part per billion or whatever that may be an accepted or unaccepted, but the fact—the fact simply is—and it is frustrating for me, too—to understand that we have one agency in the Government, a scientific agency, establishing, maybe, a standard for—for dioxin in water; another, a different agency, in fish; another in another substance which they will not stand by, which will not hold up in court if that industry came in and said, "Well, we challenge your documentation, your experimentation on this because it has no validity when it comes to human beings." So I think the frustration which you feel is always felt on this side of the equation, also.

I have a problem in New York; we both have. New York Legislature, in its wisdom, this year passed a bill which would require the phasing out of all landfills, garbage disposal landfills, by 19—I believe it is 1990. Garbage is not going to go away. The only way, I guess, to get rid of that garbage is if you export it to some other State that doesn't have that kind of law or go to resource recovery plants.

And I know of none in the United States, including one in my district, that does—that is working at this particular point in time. The one in my district was closed because of a study, an EPA evaluation that was done which showed an emittent, a dioxin emittent, a part per trillion, which could not have been measured, maybe, some years back. The point I guess I'm trying to make is that seemingly, along with the research, necessarily there must be some risk analysis that—why this is unacceptable, this is more unacceptable.

I just share with you—maybe you'd like to, you know, comment on my frustration, also, but the fact is simply we've gone through thousands, millions of dollars worth of—thousands of studies, and yet here we are, as you said, in the end of August—of July 1983, and we can't make a determination that can be backed up legally.

Mr. SCHEUER. Would you make that a brief answer, Dr. Selikoff, and we'll try to get one more member before the rollcall vote.

Dr. SELIKOFF. Sure. One of the reasons that you have these differences of opinion is the part per trillion that you mentioned is not a single exposure. It's part per trillion today; part per trillion tomorrow; part per trillion the next day and since dioxin is cumulative, and its effects are cumulative in the human body, we have very great difficulty in knowing what parts per trillion really mean.

Second, you mentioned millions of dollars. There have been several millions of dollars already spent on dioxin research, but you know, what the Government just spent in Times Beach—$30 million—is far more buying that town than all dioxin research that has ever been done since 1957.

Mr. MCGRATH. I am not suggesting that we've done enough. I am just saying that what we've done, we've not been able to use.

Mr. SCHEUER. Congressman Harold Volkmer.

Mr. VOLKMER. Dr. Selikoff, I get, too, from the gist of your testimony is that, as of this time right now, we have—really no hard evidence in this country through our research that the dioxin we're talking about here has caused cancer. In other words, definitely proven that it caused cancer; is that correct?

Dr. SELIKOFF. No. I think that the soft tissue sarcomas that have been found in these plants show that dioxin—work in those plants—can be related to human cancer. What has not been done is how much human cancer, at what level, what kinds of human cancer. That is virtually unknown.

Mr. VOLKMER. All right. And do we know the degree of exposure, et cetera, that is necessary to cause soft tissue sarcoma?

Dr. SELIKOFF. No. We do not know. Our laboratory, in 1977, examined several hundred workers at the Monsanto plant in Nitro, W. Va. We were anxious to see how their health related to the work that they had since 1949 when an accident occurred—it was never published, but it occurred—in the Monsanto plant. They discontinued making 2,4,5-T in 1969.

When we look to see how much dioxin exposure had occurred, there were no data whatsoever. No measurements had ever been made—in the nature of things, I am not blaming Monsanto. Nobody was going to measure it when they were not quite sure it had much relationship. But there are no data on what the exposures have been over the years that might be related to the diseases now being seen.

Mr. VOLKMER. I quite agree with you that we need additional research. In my opinion, we can't do too much of it, and it is not only in the field of the health effects of dioxin, but being as one from Missouri where we have the thing spread around by a man mixing with oil and spraying all over the dirt, including some in my district and almost every part of the State, the question of degradation and how do you remove it and what do we do about it also still remains—

Dr. SELIKOFF. Tremendously important.

Mr. VOLKMER. And there has been very little research done in that.

Dr. SELIKOFF. Absolutely.

Mr. VOLKMER And we need additional research. I appreciate your testimony here today. Is there any way that we could possibly coordinate the research that undoubtedly is going on? In other words, we got NIOSH getting into it; EPA, Air Force, various groups getting into it. Is there any way that can be—do you suggest, anyway, that it be coordinated?

Dr. SELIKOFF. Yes, the Department of Health and Human Services does have an overall—not only responsibility, but capability—of coordinating studies that are being done, let us say, at the National Institute of Environmental Health Sciences and other NIH agencies. I don't know how much they coordinate with EPA, but there has been little health effects research on dioxin, or virtually anything else at EPA, so that won't be much of a problem. Maybe now it will be a problem with Mr. Ruckelshaus there because perhaps there will be much more health effects research than there has been in the past.

But such coordination is well within the capability and interest of the Department of Health and Human Services.

Mr. VOLKMER. One last thing that in my brief exposure—in other words, to the question of dioxin that has been lately brought up to the public, especially in Missouri, but I think it should have been known way back—there was other comments then, but anyway, in some of the articles I have read, it seems to have even a various effect on animals. Different animals have different effects from dioxin and can you comment on that and how do we explain this?

Dr. SELIKOFF. We don't know how to explain that. We know very little about what the effects are, the mechanisms of the effects, in animals. For example, when the Seveso disaster occurred in 1976, 2 days later, when the health workers went into the field to see what was happening, there were rabbits lying dead; they had been eating the leaves that had been contaminated with the dioxin. Postmortems were done in these animals, and after the postmortems, they had no idea of why the animals died. We still don't know why guinea pigs die when they are exposed to a few molecules of dioxin.

But this is not unusual. In 1973, 1974, when the PCB disaster occurred in Michigan—you remember the polybrominated biphenyls—when the cows and the chickens were autopsied, they had no idea why these animals died, and when the farmers complained of adverse symptoms, well, they were called malingerers. Well, if we did postmortems on the animals that didn't know why they died, I don't see why anybody should have called these farmers malingerers. They weren't well; they knew they weren't well. These were God-fearing, hard-working people and they weren't well.

So that we haven't done those studies. We know that it affects cells; we know that it's cumulative; we know that it totally changes the enzymes of the body, the whole metabolism of the body, which then affects everything else, so the enzyme induction is well know, but we don't know how this ultimately results in cancer or birth defects or liver disease, et cetera.

That kind of basic research is also badly needed and should go along, but as I say, not before—or not instead of, but together with the urgent human effects research.

Mr. VOLKMER. Do we also find different effects on when it is ingested as when it is just exposed to the skin?

Dr. SELIKOFF. I think——

Mr. VOLKMER. On animals.

Dr. SELIKOFF. I think so. It can come in through the skin; it can be inhaled. That is why particles of dust from a site or a road—it can come in through ingestion. Sometimes it comes all ways.

For example, in your State, sir, at Times Beach, we were worried about the dust being taken from the road to houses blocks away but nobody looked at the gas company workers who had, for 6 months, been digging pipe, laying pipe through these contaminated soils. Very often they would have to fix—weld something on their machinery. Nobody looked to see what was happening with the high heats. Nobody asked, were they taking their clothes home? There were literally hundreds of gas company workers in Times Beach laying pipe through these contaminated soils and my guess

is that they were being exposed by inhalation, by ingestion and through their skin.

Mr. VOLKMER. Thank you very much. We have a vote on. We will recess until about 10 minutes until 11. Thank you very much.

[Recess.]

Mr. SCHEUER. All right.

Dr. Selikoff, we appreciate your patience and the committee will come to order again. We may have—we have been joined by Congressman Tom Lewis of the State of Florida, very active and involved member of this subcommittee.

Dr. Selikoff, on the Ranch Hand study, what is your assessment of the results that we can expect from it and their value and their cost compared to the results that we can expect from the NIOSH study and their value and their cost?

Dr. SELIKOFF. I don't think they're competitive. What NIOSH is doing will give us one type of information; what the Air Force is doing will give us another type of information. I've had the opportunity of seeing what the Air Force is doing and I'm tremendously impressed in the quality of the work that's being done. The Air Force has assembled an extraordinarily competent group of epidemiologists and statisticians and physicians and an excellent piece of work is being done.

Unfortunately, we don't know what to look for because the Air Force doesn't know any more than we do about that; second, because of the small number of people that were involved, and since we have decades to wait to see what the ultimate effects are going to be, we will have to wait for those decades before information is available that will guide us.

Now, should we wait? I think we should, but I don't think we ought to sit and do nothing while waiting for the Air Force to complete its very capably done study. How much it's going to cost—I think you'd better ask the Surgeon General of the Air Force. I've heard all kinds of rumors ranging from $50 to $100 million, and knowing how things go, I would probably guess that the latter figure is most accurate.

Mr. SCHEUER. How long will it take us to get definitive results from the Ranch Hand study?

Dr. SELIKOFF. Uh, definitive results; I'm not sure we'll ever have definitive results because of the constraints under which they are working. They have only a limited number of people who are involved in the Ranch Hand operation and if something is going to occur very commonly, then we should have answers that are definitive, perhaps within the next 20 years.

If, on the other hand, we will only increase—let's say, lung cancer by 20-, or 30- or 40 percent, then we may never really have that information and when we are looking at a small number of people.

So that it will—it'll all depend upon how kind nature is to us. But whatever data are there, they're going to be very competently studied and very competently obtained.

Mr. SCHEUER. Dr. Selikoff, in testimony before our subcommittee on March 23 of this year, a Dow Co. executive, Mr. Perry Gehring, Dow's vice president for agricultural chemical research and development, and also their director of health and environmental sci-

ence, stated, "While highly toxic in certain animal systems, dioxin's hazards to humans has been overemphasized. In the absence of chloracne, there is no clear evidence that dioxin poses any risk to human health, either acutely or chronically."

Would you care to react to that statement?

Dr. SELIKOFF. Sure, Perry Gehring is an excellent toxicologist, very capable scientist. Perhaps he might have expanded his remarks a bit by saying we have no evidence of the human health effects and that would be accurate. We have very little evidence. We have no evidence to the contrary. It's the old problem that we face. The semantic problem between "there is no evidence that," and "we've studied the problem and find no evidence that."

Now, when you don't study a problem, "there is no evidence that." But that you knew before you started.

Mr. SCHEUER. Well, haven't we—is my understanding that in the NIOSH study, they studied five—they looked at the records of 5,000 workers, approximately 107 of whom had died, and of the 107 whom had died, they found that something like 20-odd times, the statistically expectable number that might have died of cancer—of soft tissue cancer—actually did die of soft tissue cancer, and that led to perhaps not a linear cause-and-effect relationship between dioxin and soft tissue cancer, but as a judgmental matter, it certainly gave a clear—let us say, early warning signal that prolonged exposure to dioxin clearly posed a threat of cancer.

Now, if that's true—and I don't want to put words in anybody's mouth on the results of that NIOSH study—I am not a scientist—but if that is a fair interpretation of the NIOSH study, it's hard to stay—it's hard to say that and say that it is not totally inconsistent with what these Dow scientists have stated.

Dr. SELIKOFF. Well, maybe Dr. Gehring didn't have that information available to him at the time.

Mr. SCHEUER. All right.

Congressman McGrath.

Mr. MCGRATH. Because it is very difficult, except recently, I imagine, to have studied the effects of dioxin in humans, and because we can measure dioxin to a greater extent than we have in the past, is there any use of going back into the past for suspected dioxin contamination and coming up with some answers to the problems based on maybe a 20-year history in the past as opposed to looking at more recent history, or future histories of studies of dioxin contamination?

Dr. SELIKOFF. Absolutely. I would do exactly that. We can, with modern recordkeeping, identify whole groups of people who were exposed—whose exposure began at long times in the past, and their experience following that start of exposure, that initiation of exposure, would be tremendously interesting and would telescope the time needed to get the answers that we want.

What you've suggested is exactly what should be done and what has been done with many other agents as well and it's a classic technique that has been very successful. NIOSH is absolutely capable of doing it. There are many other good scientists who can do this and I would strongly suggest that it be done as rapidly as possible.

However, I also think that we can simultaneously do the next thing, and that is, prevent additional dioxin exposure.

Mr. McGRATH. How legitimate or reliable, scientifically, would the results of that kind of a study be?

Dr. SELIKOFF. It would be very, very reliable. It was precisely that kind of study by the American Cancer Society that pinned down the effects of cigarette smoking and the production of lung cancer and they have a cancer prevention study which began in 1960 in which they registered 1 million people. They didn't get them when they were 10 years old; they only registered people over 40, but they asked the question, "When did you begin smoking," and then, as they followed them prospectively afterwards, they were able to define all of the characteristics which led to lung cancer with cigarette smoking.

What you have suggested is a very reliable technique.

Mr. McGRATH. I thank you.

Mr. SCHEUER. Just to fill up the record——

[Laughter.]

Mr. SCHEUER [continuing]. To clarify for the record, are you aware of any of the studies, any of the studies on this matter that indicate that dioxin is not a health hazard to human beings?

Dr. SELIKOFF. No. But you know, it is very difficult to prove a negative. My hope is, let's keep our fingers crossed that we will find ultimately, after we examine the question, that dioxin will not prove to be a very serious health hazard.

We should all have our fingers crossed, but what if we're wrong? I don't think that crossed fingers are an adequate protection for the American public. For example, there are studies that are now badly needed on how to get dioxin out of the human body. Is this possible; sure, it's possible.

We showed that with kepone—you may remember the kepone difficulty in Virginia some years ago when the pharmacologists at the University of Virginia were able to develop methods of removing kepone from the human body. We should have more pharmacological research to develop that technique on getting dioxin out—and by the way, if it works with dioxin—and I look forward to it also working with PCB's and probably with PBB's.

We did a study in 1978 in Michigan which was 4 years after their PPB disaster. During 1973–74, their food supply, their dairy food supply was unfortunately contaminated. The milk, the cheese, the eggs. When we came back in 1978, at the request of the Governor of Michigan and we tested 1,800 people and we found that approximately 95 to 98 percent of all the people in Michigan still had PPB in their tissues. That was 4 years after and pharmacologically, that means it will probably be there for the rest of their lives.

If we are successful in studying how to get dioxin out of the human being, we'll also be able to utilize that for the people of Michigan, for the rest of us in our country who have PCB's in our tissues, people who have polychlorinated byphenyls, et cetera. So it is not that this piece of research or that or the other should be done, but rather, in this critical time, that all of these should be done at one time.

This is very much like the situation now with A-I-D-S, with AIDS, where all kinds of research are required and where all kinds of research are needed to solve a critical problem.

Mr. SCHEUER. Congressman Tom Lewis.

Mr. LEWIS. Thank you, Mr. Chairman.

Dr. Selikoff, you mentioned PCB's and we can go back in the early 1960's—rather, during the 1960's and the early 1970's, PCB was a miracle heat transfer agent used throughout industry. Then, I believe it was in about 1975, it had a problem creating cancer in various tissues of the body.

Is there any way—now we are looking and we are seeing the same reflection with dioxin—is there any way that upfront that we—before these transfer agents or any of these type of fluids are used or compounds are used that we could require tests prior to this? At least to have some suspect where there is a possibility of a cancer trace agent?

Dr. SELIKOFF. Mr. Lewis, that was exactly the perspective that our Congress had some years ago when it passed the TOSCA Act, saying that as chemicals are produced by industry, before they are introduced, they should be tested. It made very good sense. It hasn't been done; TOSCA has been a dismal failure. Only a handful of chemicals have ever been tested and even at that, I still would be wondering if we had the information, after all there have been hundreds of thousands of Ames tests done, thousands of animals have been sacrificed, the problem will still remain: How do you translate what you see in the test tube or the petri dish or in the cage to what is likely to happen in human beings?

But the suggestion that you make is very valid; that we do test whatever we can to see whether the replacement substances carry the same hazard, or possibly even greater hazard, than what is being replaced. I don't know whether that has been done by the companies that have made new fluids for the transformers and capacitors that were formerly filled with the PCB-containing materials.

Mr. LEWIS. Thank you, Doctor.

Mr. SCHEUER. Well, thank you very much, Dr. Selikoff, you have been very generous with your time in coming down here and you've been a forthcoming, highly intelligent witness. We appreciate it very, very much.

We probably will ask you some more questions in writing for the record.

Dr. SELIKOFF. Thank you.

Mr. SCHEUER. All right. Our next panel—if you would come up to the table, please.

Dr. Edward Brandt, Jr., Assistant Secretary for Health, Department of Health and Human Services; Dr. Vernon Houk, Director, Center for Environmental Health, Centers for Disease Control in Atlanta; Dr. Philip Landrigan, Director of the Division of Surveillance, Hazard Evaluations and Field Studies, National Institute for Occupational Safety and Health.

We are very happy to have all of you here today. We are especially happy to have Dr. Brandt back before us as a witness, so Dr. Brandt, since you're the top policymaker among us in health policy at the Department of Health and Human Services, why don't you lead off the battalion and give us your testimony.

Dr. BRANDT. Thank you very much——

Mr. SCHEUER. Your prepared testimony will be printed in full, of course, and you can proceed as you wish.

STATEMENTS OF DR. EDWARD BRANDT, JR., ASSISTANT SECRETARY FOR HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES; DR. VERNON HOUK, DIRECTOR, CENTER FOR ENVIRONMENTAL HEALTH, CENTERS FOR DISEASE CONTROL, ATLANTA, GA.; PHILIP LANDRIGAN, DIRECTOR, DIVISION OF SURVEILLANCE, HAZARD EVALUATIONS AND FIELD STUDIES, NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH, ACCOMPANIED BY MARILYN FINGERHUT, EPIDEMIOLOGIST, PROJECT OFFICER DIOXIN REGISTRY STUDIES

Dr. BRANDT. Thank you very much, Mr. Chairman. I will try to summarize the testimony. You have introduced my colleagues who are here with me.

It is important to recognize that there are 75 related compounds generally referred to as dioxin. Our testimony today will relate specifically to the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin, otherwise known as TCDD, which I think is generally recognized to be the most toxic.

Public Health Service is doing a considerable amount of work relating to the known and potential health effects of exposure to this compound. I would like to summarize the work that is going on throughout the Public Health Service.

Most of the information on health effects, as you know, comes from extensive animal studies, and from some studies of workers inadvertently exposed to dioxin-containing products. It is generally agreed that dioxin can cause chloracne.

In addition, porphyria cutanea tarda, an acquired form of porphyria characterized by chronic skin lesions and other symptoms, has been observed in some instances after dioxin exposure.

There is an increasing body of evidence that there may be an association in workers between exposure to products containing dioxin and soft tissue sarcoma. However, further studies are necessary before we can determine whether or not this association is causal. Results thus far are not sufficient to establish a cause-and-effect relationship.

The National Institutes of Health, and specifically the National Cancer Institute, have conducted studies that indicate that although dioxin was carcinogenic by oral administration, when applied to the skins of mice, it was not carcinogenic for male mice, but was for females. Currently, NCI is conducting epidemiologic studies in groups of workers who were exposed to various herbicides which may have been contaminated with dioxin. These studies are specifically investigating the incidence of soft tissue sarcoma in farmers and in others who have used herbicides.

The NCI also funds two grants investigating the effects of dioxins on hepatic microsomal enzymes, and a grant studying the relation-

ship between cancer incidence and phenoxy herbicide exposure in 13 counties of western Washington State. The National Institute of Environmental Health Sciences has evaluated the toxicity of dioxin in animals using conventional pharmacological and toxicological procedures.

They have learned that in general, dioxin produces a characteristic pattern of short-term toxic effects that involves skin, liver and the immune system in animals. However, it does not appear that exposure to dioxin produces adverse genetic effects, alters fertility in male rodents, or increases the incidence of malformed offspring sired by treated males. Several independent studies in experimental animals also have revealed that dioxin is carcinogenic in those animals.

While there are human data that document the immediate or short-term effects of dioxin exposure, the long-term sequelae are not as well understood. One study being supported by the National Institute of Environmental Health Sciences to enhance the sample size associated with industrial exposure—the International Dioxin Registry, which is being coordinated by the International Agency for Research on Cancer, of the World Health Organization, and that is being done with funding provided by that institute.

It has been observed that dioxin has a natural tendency to bind to components of soil. Some scientists speculate that in such an instance, the toxicity potential of dioxin would be diminished. If dioxin bioavailability is appreciably diminished due to binding in soil, it may have practical utility in assessing risk associated with levels in the environment.

We have under way a series of experiments in progress at the National Institute for Environment Health Sciences to study dioxin bioavailability from soil. These studies are in animals.

The Food and Drug Administration is involved in the dioxin issue because of concern over contamination of certain species of fish in the Great Lakes area. In 1981, after a thorough review of all the available human epidemiology and animal toxicology data, FDA provided a public health advisory to the State of Michigan and the other Great Lake States.

This advisory stated that based on the animal data from several studies and data on human consumption of fish, FDA would not consider fish with residues of 25 parts per trillion or less to pose a human health hazard. And, indeed, fish which averaged 25 to 50 parts per trillion should not be eaten more than twice a month by individuals who usually eat locally caught fish.

Fish containing more than 50 parts per trillion should not be consumed. Should any new scientific evidence become available to change these decisions, the agency is fully prepared to do so.

The Centers for Disease Control is conducting a large-scale agent orange epidemiology study, as mandated by Public Law 96-151. This study involves three separate but related investigations: One, to evaluate the possible long-term health effects of exposure of U.S. ground forces to agent orange; a second, to make an assessment of the possible health effects of service in Vietnam; and a third, to assess the potential association between service in Vietnam and soft tissue sarcoma and lymphoma.

The CDC birth defects study may be able to determine whether there is an association between birth defects in children and service of their fathers in Vietnam, where they may have been exposed to agent orange.

In response to dioxin environmental contamination incidents, such as those in Missouri, Michigan, New Jersey, CDC has regularly issued health advisories and is working with State and local health departments, as well as the EPA, to provide studies of the affected populations to help determine what, if any, human health effects occurred as a result of exposure.

CDC's National Institute for Occupational Safety and Health has conducted studies of the health effects of dioxin on workers involved in the manufacture of products contaminated by the compound. In response to your specific request, Mr. Chairman, Dr. Philip Landrigan will focus on the NIOSH work in this area. We will then be happy to respond to any questions that you may have.

[The prepared statement of Dr. Brandt follows:]

STATEMENT BY EDWARD N. BRANDT, JR., M.D., ASSISTANT SECRETARY FOR HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

I am Dr. Edward N. Brandt, Jr., Assistant Secretary for Health, Public Health Service, Department of Health and Human Services. I am accompanied by Dr. Vernon N. Houk, Director, Center for Environmental Health, CDC, Atlanta, Georgia; Dr. Philip J. Landrigan, Director, Division of Surveillance, Hazard Evaluations, and Field Studies, CDC/NIOSH, Cincinnati, Ohio; and Dr. Marilyn Fingerhut, CDC/NIOSH, Cincinnati, Ohio.

It is important to recognize that there are 75 related compounds generally referred to as dioxin. Our testimony today relates specifically to the toxicity of 2,3,7,8,-tetrachlorodibenzo-p-dioxin (TCDD), the most toxic. Exposure to dioxin is a very important public health problem and the Public Health Service is doing a considerable amount of work relating to the known and potential health effects of exposure to this compound.

Most of the information on health effects comes from extensive animal studies and from some studies of workers inadvertently exposed to dioxin-containing products. It is generally agreed that dioxin can cause chloracne. In addition, porphyria cutanea tarda, and acquired form of porphyria characterized by chronic skin lesions and other symptoms, has been observed in some instances after dioxin exposure. Industrial workers inadvertently exposed to dioxin have complained of weight loss, easy fatigability, aching muscles, insomnia, irritability, and loss of libido but these complaints are very difficult to evaluate. Also, after such exposure, abnormal liver function tests have been reported in association with tender liver and liver enlargement. Neurological changes in sensory function have been observed. There is an increasing body of evidence that there may be an association in workers between exposure to products containing dioxin and soft tissue sarcomas; however, further studies are necessary before we can determine whether or not this association is causal. Results thus far do not establish a cause and effect relationship.

A great deal of research on the health effects of dioxin is under way in the Public Health Service.

The National Institutes of Health's National Cancer Institute (NCI)'s studies have indicated that although dioxin was carcinogenic by oral administration, when applied to the skins of mice it was not carcinogenic for male mice; however, it was for female mice. Currently, NCI is conducting epidemiological studies in groups of workers who were exposed to various herbicides which may have been contaminated with dioxin. These studies are investigating the incidence of soft tissue sarcoma in farmers and others who have used herbicides.

At present, NCI maintains reference samples of dioxins. The Institute also funds two grants investigating the effects of dioxins on hepatic microsomal enzymes, and a grant studying the relationship between cancer incidence and phenoxy herbicide exposure in 13 counties of western Washington State. NCI also supports an intramural study concerning the suspected role of herbicides in causing soft tissue sarcomas.

NIH's National Institute of Environmental Health Sciences (NIEHS) has evaluated the toxicity of dioxin in animals using conventional pharmacological and toxico-

logical procedures. Because of its biological potency, dioxin also has been employed extensively as a model toxin in a variety of basic research toxicologic studies including mutagenesis, carcinogenesis and teratogenesis studies. NIEHS has learned that, in general, dioxin produces a characteristic pattern of short term toxic effects that involves skin, liver, and the immune system in animals. In addition, when administered to pregnant animals, dioxin can cause fetal toxicity and fetal death. However, it does not appear that exposure to dioxin produces adverse genetic effects, alters fertility in male rodents, or increases the incidence of malformed offspring sired by treated males. Several independent studies in experimental animals also have revealed that dioxin is carcinogenic. In addition, two separate laboratory research techniques have shown that dioxin is a potent promoter of chemically induced cancer. The biological potency of this chemical has intrigued scientists and continues to stimulate NIEHS research into the mechanism by which it produces its effect(s).

While there are human data that document the immediate or short term effects of dioxin exposure, the long term sequelae are not as well understood. One study is being supported by NIEHS to enhance the sample size associated with industrial exposure—the International Dioxin Registry being coordinated by the International Agency for Research on Cancer, of the World Health Organization, with funding provided by NIEHS.

Recent events in Missouri, Michigan, and New Jersey demonstrate that there are dioxin contaminated environments to which the public may be exposed and that the number of contaminated sites being detected is increasing. It has been observed that dioxin has a natural tendency to bind to components of soil. Some scientists speculate that in such an instance the toxicity potential would be diminished. If dioxin bioavailability is appreciably diminished due to binding in soil, it may have practical utility in assessing risk associated with levels in the environment. A series of experiments currently is in progress at NIEHS to study dioxin bioavailability from soil.

Food and Drug Administration (FDA) involvement in the dioxin issue stems from concern over contamination of certain species of fish in the Great Lakes area. In 1981, after a thorough review of all the available human epidemiology data and animal toxicology data, FDA provided a public health advisory to the State of Michigan and to other Great Lakes states. This advisory stated that based on the animal data from several studies and data on human consumption of fish, FDA would not consider fish with residues of 25 parts per trillion (ppt) or less to pose a human health hazard. Fish which averaged 25–50ppt should not be eaten more than twice a month by individuals who usually eat locally caught fish. Fish containing more than 50 ppt should not be consumed. Should any new scientific evidence become available to change these decisions the agency is fully prepared to do so.

The Centers for Disease Control, as you know, is conducting a large-scale Agent Orange epidemiology study mandated by Public Law 96–151. This study involves three separate but related investigations: One to evaluate the possible long term health effects of exposure of U.S. ground forces to Agent Orange; a second to make an assessment of the possible health effects of service in Vietnam, a third to assess the potential association between service in Vietnam and soft tissue sarcoma and lymphoma. Each of the first two studies will include a mortality assessment to determine which veterans may have died since being discharged and the causes of their deaths; a health interview; and a comprehensive medical examination and laboratory assessment. The CDC Birth Defects Study may be able to determine whether there is an association between birth defects in childern and service of their fathers in Vietnam where they may have been exposed to Agent Orange.

In response to dioxin environmental contamination incidents, such as those in Missouri, Michigan, and New Jersey, CDC has issued health advisories and is working with State and local health departments to provide studies of the affected population to help determine what, if any, human health effects have occured as a result of exposure to dioxin.

CDC's National Institute for Occupational Safety and Health (NIOSH) has conducted studies of the health effects of dioxin on workers involved in the manufacture of products contaminated by the compound. In response to your request, Dr. Landrigan will focus on the NIOSH work in this area. We will then be happy to respond to any questions you may have.

NIOSH DIOXIN STUDIES

I am Dr. Philip Landrigan, Director of the NIOSH Division of Surveillance, Hazard Evaluations, and Field Studies. With me is my NIOSH colleague, Dr. Mar-

liyn Fingerhut. I am pleased to describe today studies conducted by NIOSH which relate to long term health consequences among workers exposed to dioxion-contaminated products.

As you know, NIOSH was established by the Occupational Safety and Health Act of 1970, and charged with conducting research in matters affecting the health of workers. It is in the performance of this study that the following studies are being conducted. I will describe the NIOSH Dioxin Registry and Mortality Study and I will summarize other research involving the relationship of soft tissue sarcoma to dioxin exposure.

First let me say, however, that contrary to recent press reports on the NIOSH studies that suggest that they contain new information, the work I will describe to you is not new. Further, this work only suggests an association. Much of this work has been published in the scientific literature over the past two years. While it certainly represents a significant addition to the growing body of evidence which supports a link between dioxin exposure and soft sarcoma, there is still need for additional study in this area.

The NIOSH Dioxin Registry will provide a unique cohort of workers who are known by company records to have actually worked in chemical processes which generated dioxin as a contaminant. It is a listing of information for all U.S. production workers potentially exposed to dioxin during the synthesis of products such as trichlorophenol, 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), or pentachlorophenol. Enrollment of workers into the Registry will be completed by December 1983. We have already identified 5,000 production workers exposed to dioxin at ten U.S. facilities. We are currently evaluating exposure and record systems at four additional sites. When the Registry is completed, we expect to have identified at least 6,000 workers.

Based on the presence of several hundred cases of chloracne in workers in the Dioxin Registry, it is clear that many had a high exposure to dioxin. Additionally, many individuals worked for twenty or more years in these processes. This group constitutes a unique study population of persons with documented exposure and provides an opportunity to conduct several studies to address health outcomes of those environmentally exposed.

The mortality study, which is under way, tests the hypothesis that deaths from soft tissue sacroma or other cancers may be associated with dioxin exposure. To supplement the information provided by that study, which by definition is limited to evaluation of decreased workers of the cohort, we are planning also to obtain detailed information on the occurrence of past and present illness, including cancer, in the living members of the cohort.

In the first stage of this effort, a pilot questionnaire and medical study would be conducted for about 500 dioxin workers and a reference group of a comparable number of non-exposed workers. This study will investigate the incidence of cancer in this population, as well as the presence of skin, liver, neurological and immunological effects many years after exposure. The results of the pilot study would determine whether the questionnaire and/or medical examination should be conducted for the entire cohort of at least 6,000 persons and a comparison group.

NIOSH has also been active in reviewing the occupational literature concerning soft tissue sarcoma. In 1977, cases of soft tissue sarcoma were reported among Swedish lumberjacks who had previous exposure to phenoxy acid herbicides, which are contaminated by dioxin. This clinical observation led researchers in Sweden to conduct two separate epidemiologic case control studies. Both studies found that persons with occupational exposure to phenoxy acids had a five to six-fold increased risk of developing a soft tissue sarcoma.

Subsequent to the publication of these studies by Swedish researchers, three studies were conducted in U.S. manufacturing plants of workers exposed to the herbicide 2,4,5-trichlorophenoxy acetic acid (2,4,5-T) or its chemical precursor, trichlorophenol. Each study concluded that no excess was found in total mortality or in deaths from malignant neoplasms. However each study was small and had little chance to detect rare causes of death. We reviewed the data from these three cohorts and added the results from a fourth unpublished study and presented our findings in the medical journal, The Lancet, in July 1981. In essence, we found that three deaths, 2.9 percent of the total 105 deaths in the merged cohorts, were due to soft tissue sarcoma, where only 0.07 percent of deaths was expected to be due to this cause. A fourth individual in one of the cohorts died recently of a soft tissue sarcoma. That brings the total to four soft tissue sarcoma deaths in the four U.S. cohorts. Three additional persons who worked at 2,4,5-T production facilities were reported by their physicians to have soft tissue sarcoma. We believe it is important to evaluate the exposure and diagnosis for each individual. Accordingly, we have obtained work history records for each person from his place of employment and we have

sent pathologic tissue specimens to the Armed Forces Institute of Pathology for Review.

Mr. Chairman, this concludes my summary of the NIOSH dioxin studies. We would be happy to answer any questions you or other members of the subcommittee may have.

Mr. SCHEUER. Dr. Landrigan.

Dr. LANDRIGAN. Good morning, Mr. Chairman.

I am Dr. Philip Landrigan. I am a physician and Director of NIOSH's Division of Surveillance, Hazard Evaluations, and Field Studies, located in Cincinnati. With me, already introduced, is my colleague, Dr. Marilyn Fingerhut, an epidemiologist in our division who has been the project officer directly responsible for our dioxin registry studies.

This morning, I am pleased to discuss with you studies which we have conducted which relate to the long-term health consequences among workers exposed to products containing dioxin. In particular, I will describe the dioxin registry and the associated mortality study and also, I shall summarize other research which has investigated the relationship between exposure to dioxin and the subsequent occurrence of soft tissue sarcoma.

First, however, I should like to state that contrary to some recent press reports on our studies which suggest that they contain new information, the work I shall describe to you this morning is not new. Rather, it represents a compilation of material which was published previously. Much of it was published in the medical literature approximately 2 years ago.

Further, this work only suggests an association. While it certainly represents a significant addition to the growing body of evidence which supports a link between exposure to dioxin and the development of soft tissue sarcoma, there is clearly still a need for additional study in this area.

The NIOSH dioxin registry consists of a cohort of workers whom we have identified by company records as having worked in chemical processes in which dioxin was generated as a contaminant.

The Registry is a listing of information on all U.S. production workers who were potentially exposed to dioxin during the manufacture of such products as trichlorophenol, 2,4,5-T, a herbicide, or pentachlorophenol. Enrollment of workers into the registry is still proceeding. We have already identified approximately 5,000 workers who were exposed to dioxin at 10 facilities in the United States. Four additional sites are being evaluated now. When the registry is completed, we expect to have identified at least 6,000 workers, perhaps closer to 7,000.

Already, based on the presence of several hundred cases of chloracne in workers in the dioxin registry, it is clear that this subgroup of workers with chloracne had high exposure to dioxin. Further, many individuals in the registry worked for as long as 20 years in processes involving potential for exposure to dioxin. This subgroup, again, constitutes a population with documented heavy, long-term exposure and the existence of this subgroup provides us with an opportunity to conduct detailed medical studies to address health outcomes.

The mortality study, which is already under way, tests the hypothesis that deaths from soft tissue sarcoma, or from other can-

cers, or for that matter, for other causes of death, may be associated with exposure to dioxin. That study is not yet completed, but it's proceeding.

Also, to supplement the information which will be provided by the mortality study, which, of course, by definition is limited to evaluation of deceased workers, we are planning also to obtain detailed medical information on the occurrence of past and present illness, including cancer, among the living members of the cohort.

In the first stage of this medical effort, the pilot questionnaire and medical study will be conducted in approximately 500 dioxin workers and also in a comparison group of a roughly equal number of workers who have not been exposed to dioxin. This study will investigate the occurrence of cancer in the population and also the occurrence of skin disease, liver disease, neurological disease, immunological effects which might have occurred many years after these workers' exposure to dioxin.

We have also been actively engaged in reviewing the published medical literature concerning dioxin and soft tissue sarcoma. There was a previous report in 1977 in which cases of soft tissue sarcoma were reported among lumberjacks in Sweden who had had exposure to the phenoxy herbicides while working in the forest. Those herbicides appear to have been contaminated by dioxin.

The observation of sarcoma in those lumberjacks led researchers in Sweden to conduct two further epidemiologic studies, both of these studies found an association between occupational exposure to the phenoxy herbicides and the occurrence of soft tissue sarcoma.

Subsequent to the publication of those studies by the Swedish researchers, three studies were conducted in manufacturing plants in the United States of workers exposed to the herbicide 2,4,5-T, or its chemical precursor, trichlorophenol. Each of these studies concluded that no excess mortality from cancer had occurred among the exposed workers. However, each of those studies was small; each had but little chance to detect rare causes of death.

Our group reviewed and compiled the data from those three cohorts and also added the results of a fourth unpublished study. We presented those findings in the form of a letter to the editor of the medical journal entitled "The Lancet," and that letter to the editor was published in "The Lancet" in 1981.

In essence, we found that three deaths, that is, 2.9 percent of the total of 105 deaths which had occurred in the merged cohorts, were due to soft tissue sarcoma. By contrast, only 0.07 percent of the deaths would have been expected on the basis of national mortality statistics to have been due to soft tissue sarcoma.

Subsequent to the publication of that brief report of ours in "The Lancet," a fourth individual in one of the cohorts has died of soft tissue sarcoma. His death brings the total number of soft tissue sarcoma deaths in the U.S. cohorts to four.

Further, three additional persons who worked at 2,4,5-T productions facilities were reported by their physicians in the form of a series of letters to the editors of medical journals to have died of soft tissue sarcomas.

Our institute is in the process now of evaluating the exposure and the diagnosis in each of these individuals. In that process, we

have obtained work history records for each person from his place of employment and we have obtained pathologic tissue specimens from the hospitals where the persons were originally diagnosed and we have transmitted those tissue specimens to the Armed Forces Institute of Pathology for review.

Mr. Chairman, this concludes my summary of the NIOSH dioxin studies. Dr. Fingerhut and I are happy to answer any questions.

Mr. SCHEUER. Thank you, Thank you very much, Dr. Landrigan.

Dr. Landrigan, you are quoted in the Washington Post this morning on page 2 as follows: "The evidence is very strongly suggestive that occupation exposure to dioxin can cure—can cause cancer." I am reading from the Washington Post.

Dr. LANDRIGAN. Yes, sir.

Mr. SCHEUER. Is that an accurate quote, and do you care to elaborate on it?

Dr. LANDRIGAN. It is accurate, but I would like to elaborate upon it.

Mr. SCHEUER. Please do, and you might give us your feeling of any research that might be done further to establish whether or not there is a link between dioxin and soft tissue sarcoma, or indeed, any other kind of cancer as the previous witness indicated there might very well be.

Dr. LANDRIGAN. Well, it is our feeling, on the basis of the epidemiologic data that I was just summarized for you, that there is an association between occupational exposure to dioxin and the occurrence of soft tissue sarcoma. I would add, however, to that that the—we certainly do not yet possess incontrovertible proof of a causal association between dioxin exposure and the occurrence of soft tissue sarcoma. The principal reason why I am a bit reserved in saying that there is an association here, but not absolute proof, has to do with the relatively small number of cases which we're discussing. The development of absolute proof awaits the occurrence, if indeed, future cases occur.

Mr. SCHEUER. Right.

When you indicated there were now four deaths out of those 105, resulting from soft tissue sarcoma, how many could you have statistically predicted?

Dr. LANDRIGAN. The—based on mortality statistics which are collected by the National Center for Health Statistics from the whole population of the United States, we would have expected no more than 0.07 percent of the cases to have died of soft tissue sarcoma.

Mr. SCHEUER. Well, I guess we're, as the prior witness stated, we're dealing in dioxin more or less at the point of our knowledge 30 years ago in smoking and cancer, and that at that time, the American Tobacco Institute and the tobacco lobby was saying "There is no cause-and-effect relationship," and even today they don't admit a linear cause-and-effect relationship between smoking and tobacco.

And I guess the mathematical statisticians would say, "There is no linear relationship, no absolute 100 percent cause-and-effect linear relationship between smoking tobacco and cancer," because we can't put human beings in a test tube; we can't put them in an absolute laboratory condition for long periods of time, and I suppose the same situation would adhere today.

But as a matter of common sense, as a matter of judgment, wouldn't you say, if there is a 0.0-something statistical likelihood of a death—and you have four of them instead of some 100ths, you have four-thousands in effect, isn't there—from that very—admittedly very limited experiment, isn't there overwhelming—at least tentative evidence that the actual life experience, or putting it tragically, death experience, has knocked the statistical predictions into a cocked hat and that we had better stop, look, and listen and do whatever amount of research has to be done of a sort of a crash basis to find out what gives here?

Dr. LANDRIGAN. Yes, clearly those findings need to be corroborated.

Mr. SCHEUER. Dr. Landrigan, can—in terms of these 10 or 12 workplaces and somewhere between 5 and 7,000 workers involved, can you provide us with the names and locations of the companies that employed production workers that are in the NIOSH dioxin study, and can you give us a description of the kind of the information that you're requesting?

Dr. LANDRIGAN. Yes; we would be prepared to submit that to the record.

Mr. SCHEUER. We'd appreciate that.

[The information follows:]

ADDITIONAL INFORMATION FOR THE RECORD

July 28, 1983, hearing: Dioxin--The Impact on Human Health
(To be inserted on page 57, line 1349, of the hearing transcript)

Companies That Employed Production Workers Included in NIOSH Dioxin Registry

Diamond Shamrock	Newark, NJ
DOW	Midland, MI
Hercules	Jacksonville, AR
Monsanto	East St. Louis, IL
Monsanto	Nitro, WV
Rhone Poulenc	Portland, OR
Syntex Corp.	Verona, MO
Thompson Chemical	St. Louis, MO
Thompson Hayward	Kansas City, KA
Vertac	Jacksonville, AR

Types of Data Requested from Companies

1. Detailed descriptions of chemical processes used in the subject plants.

2. Personnel records, medical records, and workers compensation records for all persons assigned to the chemical processes of interest.

Mr. SCHEUER. Have you been experiencing any resistance in obtaining this information from these companies, or have they been comparatively forthcoming and providing it?

Dr. LANDRIGAN. In one or two plants, we have experienced some hesitation, but no ultimate resistance.

Mr. SCHEUER. Very good. All right, very good.

Congressman Volkmer of Missouri.

Mr. VOLKMER. I just have a few questions. As I understand it, from reviewing the statements other than the possible numbers of soft tissue sarcoma that were found in the studies, do we have any

other evidence other than the Swedish possibility of soft tissue sarcoma causation by dioxin?

Dr. HOUK. I think the issue—I would like to address two issues, Mr. Volkmer, if I may.

Mr. VOLKMER. All right.

Dr. HOUK. The issue of soft tissue sarcoma is such that all of the studies to date relate to human beings taken compositely suggest it is an area that we should be concerned about. No study on people that we have to date suggests that we should not be concerned about it. That, coupled with the fact that you can produce the same kind of tumor in animal models, causes us to have concern and causes us to have—push ahead with Dr. Landrigan's study on the cohort of the NIOSH Registry to help get an answer.

It is frequently said that there are no other health effects noted in human studies, and I would dispute that. We look at some of the industrial exposures, porphyria cutanea tarda occurred—it was reported by Dr. Bleiberj in the Diamond Shamrock plant, and some of the people have that condition who did not have chloracne, and I would dispute the fact that you have to have chloracne before you can have any other chronic health disease.

There were children in Seveso an acute episode that had nerve conduction defect abnormalities that did not have chloracne. Those did not persist for a long time. There—there's evidence in some of the literature that some of the industrial workers have significant amounts of liver functional abnormalities and done by a relatively crude method of liver function studies that need to be improved upon.

These are some of the things that we are attempting to approve upon in your State and in the other States of the people who have been relatively highly exposed, as Dr. Selikoff suggested this morning, as the primary group that we are looking at with a whole battery of tests, whole batter of things to determine if there are other things that we need to look about and if we need to expand those population groups in whom we are looking.

Mr. VOLKMER. Well, I just—reading over, Dr. Brandt, in your statement on the question of soft tissue sarcoma, on page two, you say "Results thus far do not establish a cause-and-effect relationship." I just wonder, what do we mean by that? Do we mean we need further research to establish that cause and effect?

Dr. BRANDT. Well—or to either establish or disestablish, depending upon what the truth is——

Mr. VOLKMER. Yes, either way.

Dr. BRANDT. One of the dilemmas that you have is, No. 1, we are talking about occupational exposures, so we are talking about relatively high exposure as compared, let's say, to the general population that might be exposed, so that that's—and second, you're talking about some people who are exposed to a great—a fairly large number of chemicals, not just dioxin in particular. So that I think it is going to take some more time, and as a matter of fact, all we're really talking about is essentially phase 1 of the NIOSH study with these results.

It is always difficult, also, to deal with a rare disease because the problem is that finding four cases when you only expect seven-hun-

dreths of one, from a mathematical point of view, is at best suggestive, and certainly not in any way——

Mr. VOLKMER. Not conclusive.

Dr. BRANDT. Not very conclusive and it's been—we've talked about cigarette smoking a little bit, and knowing something about that, I'd like to just put on the record that the first report of cigarette smoking and lung cancer was published in 1900 by the U.S. Public Health Service and not 50—not 30 years ago, but 80 years ago, so that it's not a new finding by any stretch of the imagination.

Mr. VOLKMER. OK.

Thank you very much, Mr. Chairman.

Mr. SCHEUER. We're going to have to take a break now. We'll impose on you for about 10 minutes.

Let me just ask Dr. Houk before we leave, did you mention the children had suffered some untoward health effects from chlor—from dioxin?

Dr. HOUK. In the—the published Seveso report, there is evidence that there was decreased nerve conduction function in some of the children, and some of these children did not have—uh, things. There is some evidence that there was some abnormalities in the immune system as it was tested in those children. That's not conclusive evidence, but if there is some evidence there, it cannot be said, in my opinion, Mr. Chairman, that there is no evidence that it has not happened.

Mr. SCHEUER. If it hasn't—if there is some evidence that dioxin is affecting children and that's established reasonably clearly, isn't that conclusive evidence that we have to perceive of the dioxin problem as something far more than just a problem of safety in the work place, that this is definitely a problem of safety in the environment that affects—that can affect and can threaten all Americans?

Dr. HOUK. The Seveso incident of those children that were exposed were probably exposed in the same order of magnitude as they would have been in the work place because it was an industrial accident that exposed them outside of the plant, but they were closely around that basic plant.

But the evidence that dioxin in some of the soils in Missouri at almost a part per million, 900 parts per billion outside of a work place, would indicate that we do have to look at this very carefully in the nonworkplace situation.

Mr. SCHEUER. All right, we are going to take about a 15—12-minute break.

[Recess.]

Mr. SCHEUER. OK. Congressman Volkmer of Missouri.

Mr. VOLKMER. Yes, I have one additional question. I note that there's been research going on as to soil contaminated with dioxin and ingesting in animals. How long will it take for this type of research before we know any results?

Dr. BRANDT. Well, we—we're estimating it will take about 2 years totally before we will know. However, we are testing some of the animals with high doses. They're being tested in 2 different kinds of soil which are essentially characteristic of the types of soil that have been involved and at varying doses—it's quite possible

that at the high doses, we may have results even sooner, but our estimate is it's probably a period of two years.

Mr. VOLKMER. Two years.

Thank you very much, Mr. Chairman.

Mr. SCHEUER. Dr. Houk, I'd like to ask you a couple of questions on the Dow press release of July 27, 1983, and I'll read you the sentences and ask you to respond. Quote "In animal studies, no species have developed soft tissue cancer when fed dioxin in lab experiments."

Is this an accurate statement?

Dr. HOUK. When using the term "fed," it is an accurate statement. When using the term "In the animal studies," the national toxicology program applied dioxin to the skin of male and female mice—certain amounts over certain period of time—and in the female mice, there were statistically significant soft tissue sarcomas, specifically fibrous sarcomas of the integument that were demonstrated. In the male, they were increased in numbers that did not reach statistical significance and they occurred earlier.

I believe the statement—the inference of the statement that soft tissue sarcoma has not been demonstrated in the animal model is not an accurate statement.

Mr. SCHEUER. Uh-huh.

Another sentence reads, "In human studies, results have been mixed though the preponderance of data indicates no links between dioxin exposure and soft tissue cancer."

How would you react to that statement?

Dr. HOUK. In my own personal and professional opinion, Mr. Scheuer, I would reverse that and say that of the studies in humans, the preponderance of data make us very concerned about the association of soft tissue sarcoma and this compound in the work place of the studies being done.

As previously mentioned, there is no study that conclusively goes the other direction, and that associated with the occurrence of soft tissue sarcoma in the animal model causes us a great deal of concern, which is one of the reasons that we're moving forward rapidly with Dr. Landrigan here. We are looking at this issue very carefully in the Vietnam agent orange experience—the study with the whole component of it—to try to get an answer to what we consider is one of the very important questions.

Mr. SCHEUER. On the—going to the—I take it you're at home with mathematical statistics and—which I'm not. If, out of roughly 105 deaths, we could have expected by statistical extrapolation seven one-hundredths cases of soft tissue sarcoma deaths, and instead of seven—seven one-hundredths, in effect, we got 4,000 and seven one-hundredths, would that, to you, be an important statistical indication? Why don't I ask you to interpret that—that 54 times greater variation, albeit, from a comparatively small number of deaths, but a variation going from the expected seven one-hundredths to 4.

Dr. HOUK. The number of seven one-hundredth is derived from the national statistics and with a very rare event, there may be some underreporting, but let's say that even if there is a tenfold underreporting, we would expect to find seven-tenths deaths.

You cannot find——

Mr. SCHEUER. No, no, no.

Dr. HOUK. No, no—what to expect.

Mr. SCHEUER. It would be seven-tenths

Dr. HOUK. Yes. Seven-tenths if it were a hundred fold if there were a hundred magnitude difference.

Mr. SCHEUER. No, 10 magnitude difference.

Dr. HOUK. Right. One—Mr. Chairman, one cannot find seven-tenths deaths.

Mr. SCHEUER. That's correct.

Dr. HOUK. You either find a death or you don't find a death.

Mr. SCHEUER. Yes.

Dr. HOUK. If you don't find a death, it doesn't make it negative; if you find one death, it doesn't make it positive.

Mr. SCHEUER. Correct.

Dr. HOUK. If you find two deaths, you're a little bit more worried than one death; if you find three deaths, you're more worried than two; if you find four, you're a lot more worried than finding one.

This is why I believe that this is a suggested association. We should get on with determining and delineating this as rapidly as we can in the best abil—in the best of our ability.

Mr. SCHEUER. If I were——

Dr. BRANDT. Could I add to that just——

Mr. SCHEUER. Of course.

Dr. BRANDT [continuing]. Just one thing, and that is——

Mr. SCHEUER. You seem fairly relaxed about this before and I wonder whether, after thinking about it, that—since we can't find seven-tenths of a death, or seventy one-hundredths of a death—one would not be more, but two is a little more, and three is a little more, and four. If I were one of the chief health policymakers of the executive branch of the Government of the United States, to me the early warning system would be going up.

Dr. BRANDT. The early warning signal has gone up and we have, therefore, set forth this Dioxin Registry, and we have put into operation the—we have a total research program within the Public Health Service ranging all the way from intracellular up to epidemiologic studies involving dioxin because we want to be sure that we know what's going on.

On the other hand, I don't think there's any point in panicking at this stage of the game, because if you look just specifically at this—and you would expect seven one-hundredths deaths, and you got one, you already have a fourteenfold increase, which is nonsense.

Mr. SCHEUER. Nobody is suggesting that getting one would be meaningful.

Dr. BRANDT. Yeah, right.

Mr. SCHEUER. But as Dr. Houk suggested, when you go to two, a little more meaningful——

Dr. BRANDT. And you keep getting——

Mr. SCHEUER [continuing]. Go to three, little more meaning; four—I am suggesting that the early warning signal ought to be going up and that we ought to be deeply concerned.

Dr. BRANDT. Well, I think we are. I think that any—I mean, we are concerned; we are following up; we are—we do have studies

commissioned and we have the Dioxin Registry that NIOSH is running in an attempt to try to nail this down one way or the other.

Mr. SCHEUER. I'm told that there are--I'm just been told that there are three more of those workers who have soft tissue sarcoma who have not died yet, but that would bring the count up to seven.

Dr. BRANDT. But not—but wait a minute, you can't——

Mr. SCHEUER. But they haven't died yet and hopefully they won't.

Dr. BRANDT. We're mixing apples and oranges so that that's the kind of a—that's a red herring.

Mr. SCHEUER. I'm not sure it's a red herring, but we ought to put them in a holding pattern and hope that they won't—that that action won't be lethal in respect to the three men who have not died yet.

Nobody is trying to scare the American public. Nobody is trying to enlarge a risk that possibly might be construed as a risk inherent in the workplace to a risk inherent in our total environment if the evidence doesn't justify that. We're not trying to panic people.

On the other hand, we're not trying—we don't want falsely to assuage legitimate concerns. What we're trying to do is to tread a responsible middle road and what we're trying to do is make sure that we fine tune our thinking and develop as fast as we can the knowledge that we don't have now; to enlarge our knowledge base so that we can do, in a cost-effective, sensible fashion—we can do the regulating that—and the legislating that seems intellgent and thoughtful and responsive to the real order of magnitude of the risk without panicking and without unduly arousing people's concerns. But without——

Dr. BRANDT. Let me——

Mr. SCHEUER [continuing]. Falling to the other extreme of being Pollyannaish.

Dr. BRANDT. Right. I don't—I agree.

Mr. SCHEUER. We are not a bunch of Dr. Panglosses up here. We're trying to be responsible realists and that is something of a burden for us, as it is for you, I'm sure.

Dr. BRANDT. I—I want to assure you that we're not in any way trying to be Pollyannaish about it, nor am—but I do think—I mean, and as a consequence, we have commissioned the necessary studies to follow up on this. Our goal is to try to find out what are the real health hazards of dioxin; at what levels of exposure are we talking about; our people who live in areas where dioxin is bound to the soil at any risk at all, and if so, of what; and so forth. So we are not trying to ignore it.

On the other hand, I just think we've got to take it in a scientific stepwise fashion.

Mr. SCHEUER. Dr. Landrigan, what kind of resistance did you—did you reach—did you experience with the various chemical companies in trying to elicit information about their workers who had been involved for long periods of time with dioxin at the work site?

Dr. LANDRIGAN. OK. I'd like to begin my answer, Mr. Chairman, by reassuring you that we did ultimately get from the various companies all of the information that we sought. The companies—several of them—did, however, ask us to present our study protocols to

them in very considerable detail. They wanted to be assured and reassured that the information that they were going to turn over to us from their medical records was going to be held confidential. There were checks and rechecks and in some cases, it took us a number of months before we obtained the information.

We did, however, ultimately in every case, obtain the information and we did, ultimately get reasonable quality of cooperation from each of the companies, and it was that cooperation which enabled the work finally to go forward.

Mr. SCHEUER. Why do you think it took so long? Why do you think they hesitated?

Mr. LANDRIGAN. I don't know. I think you'd have to ask them.

Mr. SCHEUER. Were there any legitimate concerns of proprietary information involved here?

Dr. LANDRIGAN. Trade secrecy was really not the issue because we weren't dealing with processed data except peripherally. There was, however, concern about confidentiality of medical records and I think that is legitimate. After all, nobody wants to turn over medical records and have them be broadcast. However, at National Institute, we have quite a sophisticated system, a system which has not ever been breached for holding medical records secure and we were able to assure the companies of the integrity of that system.

Mr. MCGRATH. Dr. Brandt, I understand that last week you had a meeting with the heads of your major divisions of the Public Health Service to formulate a position on dioxin for the Public Health Service.

We were informed that a consensus position was reached, that the evidence is mounting that dioxin is a human carcinogen and that it should be treated accordingly.

What, then, is the official position of the Public Health Service on dioxin?

Dr. BRANDT. Well, I don't think there was any consensus, either particularly sought or reached, on many of the public health problems that face the country where work is going on throughout the Public Health Service with many of the five agencies involved. I periodically hold these meetings to try to determine where we stand, where we're going, what are we learning, and will that modify other kinds of programs.

I think what we—what I believe—and these were scientists, not necessarily the heads of the agencies, but actually the working scientists who I deal with on the question of AIDS, on the question of food safety and a whole lot of other issues that we deal with constantly, and what I think we agreed to was—or what we at least wrote down and I think was, one, there is evidence in animals, in some animals, that dioxin does cause malignancies, particularly as pointed out in rats, in the female rats, at least, that—and that we have this soft tissue sarcoma data that deserves to be followed up.

I don't think that we came to any sort of—I don't even remember that we had any discussion about whether or not it's a human carcinogen other than the issue of following up on these soft tissue sarcoma reported associations.

Mr. MCGRATH. All right. It's your responsibility——

Dr. BRANDT. By the way, that's not the first meeting we've had about this. I——

Mr. MCGRATH. I cast no aspersions.

Dr. BRANDT. OK.

Mr. MCGRATH. It's your responsibility to do the basic research regarding the effects of dioxin and hopefully come up with standards, if possible——

Dr. BRANDT. Right.

Mr. MCGRATH [continuing]. To insure the public health and safety of the American people. It's our job to legislate, in some cases, laws which protect the health and safety of people in the work place or generally.

Based on whatever information you have from various sources and various studies that have been conducted by yourselves and others, do you believe there is enough evidence to help us legislate or do you believe that we don't have enough evidence to legislate right-to-know laws in public—in work places at the present time?

Dr. BRANDT. By "right-to-know," do you mean——

Mr. MCGRATH. What I mean is that the employees have a right to know what kind of materials, toxic or other materials that they are working with.

Dr. BRANDT. I think that—that it would be difficult to write such legislation right now, largely because, in a complex working environment, it may very well not even be possible to know what all is present, much less whether or not there are any kind of health effects related to those, so I think such legislation would be, at best, very difficult to write.

In terms of dioxin, I think we are not at a stage where one could write very precise legislation that would be very helpful because of certain bits of information we don't know. Dr. Selikoff was talking about the possibility of removing dioxin. I'm much more concerned about trying to measure dioxin in people.

We have no way of knowing whether or not you or I are walking with circulating dioxins in our bloodstream. We have no way of measuring it in humans, which is one of the problems, for example, in the soft tissue sarcoma problem. We don't know that those people actually had dioxin in their bloodstream or in their tissues and so forth, because we have no way of measuring it at the present time.

That's something that we would like to be able to do ultimately, but we're a long way from doing that. There are a lot of other fundamental questions, it seems to me, that need to be answered before we can get too precise legislatively. I mean, I have no objection to people knowing what they're being exposed to; that's no problem as long as you know what it is. That, however, is sometimes a problem.

Mr. MCGRATH. Dr. Landrigan, in 1980, a Dr. Ward in England came up with a connection between a human immune system defect and dioxin exposure. Have you—has NIOSH or—or will you examine that study to find out whether or not there is any validity? At the last hearing we had, that study was somewhat panned by those who testified before us, but it is a study on which many of the Vietnam veterans groups are basing their contention that there is a link between some forms of disease found prevalent in Vietnam veterans and the exposure to dioxin.

Dr. LANDRIGAN. Mr. McGrath, Dr. Houk knows more about this than I am. I'd like to refer the answer to him.

Mr. MCGRATH. Anybody.

Dr. HOUK. The so-called Ward study is—it was in effect, Mr. McGrath, not a study; it was observations that he wrote down without a lot of—of careful standardizations—at least in the published report—and what was found because of that, and because of our interest in the Vietnam veterans issue, a member of my staff, Dr. Erickson, who is a senior scientist on that issue—met with Dr. Ward 2 weeks after Mr. Daschle had his press announcement to discuss his results and what he found and to ask his advice.

His results were not discussed—as was reported in the industry. He found some minor—his words, "some minor variations in the immunologic patterns of these people who he studied early on that did not persist." We chose the opportunity because he is an imminent immunologist who has his good advice the same as we've asked of the immunologists of our own country of what sort of studies—what sort of techniques should we be using to address this issue.

Those are being incorporated into the Vietnam veterans' study; they are being incorporated into our studies of the dioxin around this country; the domestic issues, and we will be discussing with Dr. Landigran and his group, providing them that same advice that has been provided to us and I know that they are very interested in looking at the immunologic question, too, because it is the—it is the worker group, the occupationally exposed group, who have the highest, most consistent, and most probable exposure.

Mr. MCGRATH. Thank you.

Mr. SCHEUER. Congressman MacKay.

Mr. MACKAY. No questions.

Mr. SCHEUER. Dr. Brandt, you've addressed yourself to some of the areas in which our knowledge is deficient and you're are undoubtedly right.

Dr. Selikoff mentioned a number of areas in which he expressed the urgent need to improve our knowledge basis. What plans do you have, as chief policymaker over at HHS, to acclerate the research process so that we will, in as short a timeframe as possible, have the knowledge that we need up here to deal effectively with this problem of dioxin, both from the point of view of legislating and from your point of view of administering this problem?

Dr. BRANDT. I don't think at the present time, Mr. Scheuer, there's any way we can really accelerate getting the results. For example, we have initiated the studies on bioavailability. We have initiated the registry. We have initiated studies on looking at liver enzyme changes. We have initiated studies over a broad range. Those are going to take time and I think they are underway and in the interim, as new leads develop, why, we will certainly initiate additional studies in the appropriate fashion to move them, but it is going to take us a minumum of 2 years to look at the bioavailability issue alone, just because that is the nature of the beast, as it were.

Nothing that we can do that I know of to—or that the people in a toxicology program know of—to accelerate that process. We agree

with Dr. Selikoff in the sense that the research must move on and we're attempting to do that.

He also brought up the issue of coordination and should point out that we have, really, three forms of coordination underway in Health and Human Services. I have a committee called Committee To Coordinate Environment and Related Programs [CCERP], by acronymn, that regularly meets—it's chaired by Dr. David Rall at—of the National Institute of Environmental Health Sciences and includes most of the representatives—or does include representatives throughout the Department, and they address the issue of dioxin as an environmental issue.

We have the agent orange working group that is within the Department of Health and Human Services, operating out of the Secretary's Office that involves representatives from other programs and then, as was pointed out to Mr. McGrath, I hold meetings periodically with the senior scientists who are involved in this area to try to determine where we stand so that at the present time, we are following up at least all of the leads that have been brought to my attention by any of the scientists at HHS, and I think we'll continue to do so, but I'm afraid that the time involved is longer than I care for it to be, but I don't know of any way to speed it up.

Mr. SCHEUER. You're—you're telling us that everything that could be done is being done.

Dr. BRANDT. I'm telling you that everything that I know of that could be done is being done at the present time, yes. I'm sure there are other things that could be done. I mean, almost—but at the present time, the best we can tell, we're doing everything that we know of to do.

Mr. SCHEUER. I get more of a sense of urgency and the need for additional research from Dr. Selikoff. I don't get any sense of great urgency or great concern from you and that may be the way you legitimately feel, but I think the American people are more concerned than that, and I think we're more concerned than that. I——

Dr. BRANDT. It is not the way I feel. I mean, I'm sorry I haven't—I'm not as dramatic about it, but I'm as frustrated as he is and probably more so since I think I'm in a position where I have to do something and—but on the other hand, I—we have to depend upon the best minds' advice. In my judgment, we have that and we are following their advice and we're moving it as rapidly as human biology will allow us to move it.

There are no quick answers; that's the unfortunate part. For example, we are working toward trying to figure out a way to measure dioxin in human blood. That's one of the more frustrating—it's like experiences that we've had; almost as frustrating as trying to find the causation for AIDS.

I just don't know of a way to speed up science any more than we are already doing.

Mr. SCHEUER. Do you have——

Dr. BRANDT. But I can assure you I'd love to have the answer tomorrow.

Mr. SCHEUER. Do you have anything to add, Dr. Houk?

Dr. HOUK. No; I would agree with him completely. I think that the—there are two issues—or three kinds of things that work is

going on right now, or at least on two of them. One, to find a measure of how we can measure the body burden of dioxin, what is in people. And then we get a serum test to try to see if there is a correlation between that and the fatty tissues content.

Another very significant issue that needs to be addressed is to find a way to decontaminate soil or detoxify soil. I'm not sure that very much is going on that engineeringly. But one of the most important things that we can do, I think, is in prevention. And that is to prevent more dioxin from what we already have in our environment—whether it be work-related or other-related environment—from being put in there.

We know whence the dioxin come from, from the manufacturing of certain products, the burning of certain products, and we should look very carefully to see if there are not economic alternatives to those products, that we don't allow them to be manufactured so that accidents can happen from them.

Mr. SCHEUER. You see, we're in a catch-22 situation. The EPA research budget has been cut in half by this administration, but yet, when we come to legislating or regulating, we're told we don't know enough. We may not know enough to do everything, but surely we must know enough to do something.

Maybe we don't know enough to prohibit all products that have any trace of dioxin, but don't we have a way of ameliorating the effects of dioxin in manufactured chemicals? Yet, I assure you that if we were to propose legislation tomorrow dealing with the subject that you just mentioned, we would have both administration spokesmen and chemical company spokesmen saying: "You haven't established a linear relationship between dioxin and human health effects; you haven't established a irrefutable cause-and-effect relationship between dioxin and human health effects and, therefore, it's totally unreasonable for you to want to legislate on this subject."

That's what they've been telling us on acid rain, where the clear preponderance of the evidence is that when you pollute in the Middle West, that stuff comes down in the east coast and in Canada, and decimates streams, and rivers, and lakes, and ponds, and forests, and grasslands, and croplands.

It's exactly the argument we've heard for 30 years from the tobacco industry. So in the current state of our knowledge, if we can't elicit some real anxiety and concern from Dr. Brandt over the fact that we had four deaths instead of .027—07, and we have this totally relaxed—yeah, the smug and self-satisfied attitude of the administration where they are sort of poo-pooing the implication of this, to me, astounding mathematical result here, how can you possibly expect that Congress is going to be able to legislate?

We need far more knowledge than we have now to even to begin to grapple with the subject. Otherwise, we're going to have this—the same failure to come to grips with it that we've had in coming to grips with acid rain, and tobacco, and numerous other matters on which we didn't have a linearity, a 100-percent cause-and-effect relationship between various illnesses and people.

And unfortunately, we can't raise a whole generation of Americans in test tubes or in laboratories where we have a test group in one laboratory where they spend their lives, where they are ex-

posed to X; and another test group in another laboratory where they spend their lives where they're not exposed to X, but where all of the other conditions are identical, with a mathematical exactitude.

Until that time comes, we have a very difficult problem in dealing with these things. So what we're asking is—and with some sense of urgency that we really don't find on the other side of this witness table—what knowledge do you think we ought to have in our possession up here so that we can design legislation that is sensible, that is cost-effective, that—that the data base may not justify our doing everything, but will certainly justify our doing something?

The first halting, pitiful, little, initial remedial steps, whatever they may be. This is what we want to know.

Dr. HOUK. I would like to answer—or to address, if I may, Mr. Scheuer—the first part of the question that doesn't deal with the legislative component. We are not waiting for all the answers; we cannot wait for all the answers before we make recommendations on public health policy.

As I was here on the 28th discussing how our one part per billion in soil was arrived, its assumptions to the best of our ability. We had an outside group in who basically agreed with those assumptions; that we've made recommendations in several sites in Missouri, several sites in, uh, New Jersey, relating to dioxin, PCB's, a whole host of things. We don't have the information totally, but we made recommendations to the State that, in our best judgment, are further protection of the health of the public in those particular communities.

I think that we do have a sense of urgency and I would disagree, respectfully, if I may, sir, with your perception of Dr. Brandt's sense of urgency in these matters because he is from where I get many of my instructions, and there is a sense of urgency; there is a sense of not having all the information. We're going to have to continue to make these decisions; to make these recommendations in the absence of the final dot on the "i" and the final "t," and that's the way that life is, and we are continuing basically to do that.

I—I might point out that you have as much difficulty in the other sphere, in the issue of lead. We know more about the toxicity of lead than we know about any compound in the world.

And yet, we continue to use lead in many inappropriate ways, in my view, where there are feasible alternatives that can be used instead of lead.

Mr. SCHEUER. All right. This has been a long panel and you've all showed a great deal of patience and waited through several rollcall votes. We appreciate it very much. Thank you.

We will now get on with the second panel. Mr. John Sommer, deputy—accompanied by Paul Egan—John Sommer, deputy director of the National Veterans Affairs and Rehabilitation Commission of the American Legion; Mr. Milton Milford, director of the National Veterans Law Center of the Washington College of Law at American University—we also have Maj. Gen. Murphy Chesney, Deputy Surgeon General of the U.S. Air Force.

Would Major General Chesney like to join this panel, which is dealing with the problem of the serviceman? That might expedite matters here since we are running so late.

And if you have any people you'd like to join you, they'd be more than welcome up here.

General CHESNEY. I have four people that I'd like to bring up.

Mr. SCHEUER. Well, why don't you fellows shift down a bit. All of your direct statements will be printed in full in the record.

What we would ask you to do is to summarize your statement in about 5 minutes because we are running very, very late. And then, I'm sure you've all testified, we'll have some questions for you.

So first, Mr. John Sommer.

STATEMENTS OF JOHN SOMMER, DEPUTY DIRECTOR, NATIONAL VETERANS' AFFAIRS AND REHABILITATION COMMISSION, AMERICAN LEGION, ACCOMPANIED BY PAUL S. EGAN, DEPUTY DIRECTOR, NATIONAL LEGISLATIVE COMMISSION, AMERICAN LEGION; LEWIS MILFORD, DIRECTOR, NATIONAL VETERANS LAW CENTER, WASHINGTON COLLEGE OF LAW, AMERICAN UNIVERSITY; AND MAJ. GEN. MURPHY A. CHESNEY, DEPUTY SURGEON GENERAL, U.S. AIR FORCE, ACCOMPANIED BY MAJ. JACK SPEY, RETIRED, USAF, PRESIDENT, RANCH HAND VIETNAM ASSOCIATION

Mr. EGAN. Mr. Chairman, John will summarize our remarks. I would like to point out to the committee that just this morning, the Senate—or the House Veterans' Affairs Subcommittee on Compensation and Pension has just favorably reported a bill that would afford a mechanism by which veterans could be compensated if they were able to show that they—their exposure to agent orange caused chloracne, PCT, or soft tissue sarcoma.

I would also like to add that what we've been hearing most of the morning is a good deal of equivocating. I think it's important to recognize that what that kind of equivocating causes as far as what veterans believe and feel is that somehow there's a good deal of dishonesty and if we seek to avoid a panic, particularly among veterans, and I think it's important for our policymakers to be as straightforward as possible.

Veterans are not as equivocal. They believe that dioxin is dangerous. They believe that their exposure to it has caused their various numerous maladies.

That notwithstanding what the experts say is suggested or what have you.

Mr. SCHEUER. Excuse me, going off the record. Are you John Sommer?

Mr. EGAN. I'm Paul Egan.

Mr. SCHEUER. Oh, you're Paul Egan. Who is Sommer?

Let's get these name tags up there so that—there we go. Thanks. Who is Milford? There we go. OK.

Mr. Sommer, do you wish to testify?

Mr. SOMMER. Thank you, Mr. Chairman.

Mr. Chairman, and members of the subcommittee, the American Legion certainly appreciates this opportunity to comment on the results of the U.S. Air Force Ranch Hand baseline mortality study

that were released on June 30, and on other research projects on the long-term health effects of dioxin exposure, particularly those studies relating to the exposure of Vietnam veterans to the herbicide agent orange.

It should be emphasized that the first phase of the Ranch Hand mortality determination is just as the title connotes: a baseline mortality study. The American Legion was not surprised that the mortality experience of the Ranch Hand group was not significantly different than that of the master controls at this early date.

The executive summary of the Ranch Hand report itself states.

> This baseline mortality report can in no way be regarded as conclusively negative because this small, young and relatively healthy cohort may not have yet reached the latency period wherein attributable fatal disease might be expected and detected within limited power boundaries of this study.

We are aware that the latency periods for certain types of fatal diseases, particularly malignant tumors, may extend to 20 to 30 years or longer. We found this to be true in radiation-induced cancer and mesothelioma caused by exposure to asbestos.

The insidious onset and unpredictable latency period of such diseases accentuate the importance of the morbidity portion of the Ranch Hand study and the followup studies on mortality and morbidity. It is noted in the report that the Ranch Hand group has had an increase in liver disorder deaths as compared to the mass control groups and that the enlisted members of the Ranch Hand group had experienced a higher mortality rate than the officers. We trust that a followup report will provide additional information on these two areas of concern.

Mr. Chairman, with your permission, at this point, I would like to depart from our written statement to voice the American Legion's concerns on issues regarding the Ranch Hand operations in Vietnam and the manner in which they've been described at a variety of forums over the past several years.

May I preface this by stating that the American Legion believes it is the obligation of the U.S. Government to determine, in an honest and forthright manner, the effects of agent orange on those veterans who were exposed to it in Vietnam and then to adequately compensate those Vietnam veterans who have incurred diseases and disabilities as a result of exposure.

For several years, representatives of the Air Force have made any number of presentations stating that the Ranch Hand personnel received by far the heaviest exposure to agent orange because they flew with the windows and the cargo hatches open in the C-123's that were used to spray the herbicide.

Recently, I personally had the opportunity to review extensive official film footage of Ranch Hand spraying operations that were taken during different timeframes in Vietnam. And the film also included footage of Army application of agent orange through the use of helicopters and through trucks.

Looking at this film, as I mentioned, taken over a period of years, I was unable to identify an open window or open cargo hatch in any of the C-143's in the film. In addition, the Ranch Hand aircraft flew in a formation that appeared to me to prohibit the spray from one aircraft from hitting another. No windshield wipers were operating during the entire film footage.

On the other hand, we witnessed Army helicopters, not part of the Ranch Hand operation, and who were spraying agent orange with open doors in the helicopter. In addition, the film showed Army soldiers spraying parameters from the back of open trucks with handheld hoses. None of the personnel handling the herbicide wore protective equipment.

We've also heard on many occasions that little of the agent orange spraying during the Ranch Hand operations would have reached the ground because it was released over triple-canopied jungle. Thus, the ground troops would have received little exposure.

In viewing the films, we saw little or no triple-canopy jungle. As a matter of fact, in some areas, the trees appeared to be small and sparsely located.

Mr. Chairman, this new information raises a serious level of concern in our minds as to the credibility of the Ranch Hand study. We have been led to believe that the entire crew would many times return from a mission soaked in agent orange. In the film that we saw, the pilots that were photographed all appeared to be clean.

The American Legion would be interested in knowing on what information is the claim of exposure based in the Ranch Hand study? Did the enlisted personnel receive much higher exposure than the officers? Perhaps this would shed some light on the difference in mortality between the officers and the enlisted persons.

Mr. Chairman, in closing our summary, it would be indicated that a discovery of this nature causes a great deal of frustration for us and certainly for the Vietnam veterans that we represent. For several years following the enactment of Public Law 96-151, the VA was not able to make progress in the study of agent orange for several reasons, including alleged difficulties in determining who was exposed.

While this delay continued, we were repeatedly told about the progress of the Ranch Hand study, a study of the people supposedly most heavily exposed.

Now, Mr. Chairman, I have seen documentary evidence which seriously questions the repeated assumption that the Ranch Hand personnel were heavily exposed. As stated earlier, it raises a question to us as to the credibility of the study in our minds.

Thank you for this opportunity to present our comments.

[The prepared statements of Mr. Egan and Mr. Sommer follow:]

Statement of

The American Legion

1608 K STREET, N. W.
WASHINGTON, D. C. 20006

PAUL S. EGAN, DEPUTY DIRECTOR
NATIONAL LEGISLATIVE COMMISSION
THE AMERICAN LEGION

and

JOHN F. SOMMER, JR., DEPUTY DIRECTOR
NATIONAL VETERANS AFFAIRS AND REHABILITATION COMMISSION
THE AMERICAN LEGION

before the

COMMITTEE ON SCIENCE AND TECHNOLOGY
SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE
RESEARCH AND ENVIRONMENT
UNITED STATES HOUSE OF REPRESENTATIVES

on

DIOXIN OVERSIGHT

JULY 28, 1983

STATEMENT OF JOHN F. SOMMER, JR., DEPUTY DIRECTOR
NATIONAL VETERANS AFFAIRS AND REHABILITATION COMMISSION
THE AMERICAN LEGION
BEFORE THE SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE
RESEARCH AND ENVIRONMENT
COMMITTEE ON SCIENCE AND TECHNOLOGY
HOUSE OF REPRESENTATIVES
JULY 28, 1983

Mr. Chairman and Members of the Subcommittee:

The American Legion appreciates this opportunity to comment on the results of the U.S. Air Force Ranch Hand baseline mortality study that were released on June 30, 1983; and on other research projects on the long-term health effects of dioxin exposure, particularly those studies relating to the exposure of Vietnam veterans to the herbicide Agent Orange.

The examination of Ranch Hand personnel, those Air Force personnel who were directly involved in Agent Orange spraying missions in Vietnam, has been completed, and we understand that an excellent rate of participation among the over 1200 individuals who served in that unit was experienced. The entire Ranch Hand study is composed of three elements; a mortality study, a morbidity study, and a follow-up. The questionnaire involved in this investigation was administered under contract by the Harris Organization, and the physical examinations and laboratory studies were conducted by the Kelsey-Seybold Clinic in Houston, Texas on a contract basis. As previously mentioned, the initial mortality report was issued on June 30, and preliminary reports on the data obtained from the examinations and questionnaires are expected to be issued later this year. We understand that mortality in the

study population will be determined annually for the next 20 years, and follow-up examinations will be completed at 3, 5, 10, 15 and 20 year points.

Mr. Chairman, it should be emphasized that the first phase of the Ranch Hand mortality determination is just as the title connotes - a baseline mortality study.

The American Legion was not surprised that the mortality experience of the Ranch Hand group was not significantly different than that of the matched controls at this early date. The Executive Summary of the Ranch Hand report itself states "This baseline mortality report can in no way be regarded as conclusively negative because this small, young, and relatively healthy cohort may not have yet reached the latency period wherein attributable fatal disease might be expected and detected within limited power boundaries of this study."

The Legion is aware that the latency periods for certain types of fatal diseases, particularly malignant cancers, may extend to 20-30 years or longer. We have found this to be true in cases of radiation induced cancer, and mesothelioma caused by exposure to asbestos. The insidious onset and unpredictable latency period of such diseases accentuate the importance of the morbidity portion of the Ranch Hand Study, and the follow-up studies on mortality and morbidity.

It is noted in the report that the Ranch Hand group had an increase in liver disorder deaths as compared to the matched control group; and that the enlisted members of the Ranch Hand

group had experienced a higher mortality rate than the officers. We trust that the follow-up reports will provide additional information on these two areas of concern.

Mr. Chairman, The American Legion was extremely pleased that the Centers for Disease Control took over the responsibility for the PL 96-151 study when the Interagency Agreement between the Veterans Administration and the Department of Health and Human Services was signed on January 14, 1983. The transfer fulfilled a long and intense effort by the Legion to have the study completed by a scientific agency that is independent of the VA.

We are encouraged by the manner in which CDC has progressed since accepting the responsibility for the study. Within a matter of days following the signing of the Interagency Agreement, CDC officials met with The American Legion to discuss the study and elicit input and recommendations relating to the research.

At the same time, we offered the cooperation of the Legion in encouraging the participation of Vietnam veterans in the study, as we are keenly aware of the importance that such participation will play in the success of the CDC studies.

In reviewing the protocol outline prepared by CDC when it first became available to the Legion in early February, it was obvious that a great deal of what appears to us to be highly competent work was achieved in a relatively short period of time.

CDC has recommended that two historical cohort studies be completed; the Agent Orange study, and a broader Vietnam experience study. Authority for the expansion of the study was provided

under PL 97-72, and CDC was quick to realize the importance of studying the possible health effects that other herbicides such as Agents White and Blue (picloram and cacodylic acid, respectively), other chemicals, medications, or environmental hazards or conditions, that existed in Vietnam could have had on the veterans who served in RVN.

The studies will each be comprised of three major components; a mortality study, a health and exposure questionnaire, and a clinical and laboratory assessment.

The Agent Orange study is to consist of 3 cohorts, and the Vietnam experience study 2 cohorts. The cohorts are to be composed of 6,000 individuals each, selected pursuant to a thorough review of the military records by the Army Agent Orange Task Force (AAOTF). The American Legion is pleased to have learned that CDC has assigned a Public Health Advisor to work full-time with the AAOTF, as we have long stressed the importance of a liaison between this dedicated group of experts in the area of military records and the agency responsible for the development of the protocol and the conduct of the Agent Orange study.

The AAOTF plays an integral part in the Agent Orange research efforts, and especially with respect to the foregoing studies that are currently being implemented by CDC. Without the military records from Vietnam the study cohorts could not be selected, thus it would be impossible to carry out the studies.

The Legion understands that CDC has received approval for the requested positions needed to carry out the studies, and they are

in the process of recruiting the necessary staff. However, this has not detracted from the ongoing development of the protocols for the two studies which are completed and currently undergoing peer review.

CDC is also planning to conduct case-control studies of the incidence of soft tissue sarcomas and lymphomas. The American Legion is aware of the importance of such case-control studies, particularly with respect to soft tissue sarcomas, and we strongly urge that they be conducted.

Mr. Chairman, as we stated at the outset, the Legion is both encouraged and pleased by the progress made by CDC in a relatively short period of time. In addition, CDC has held to a commitment made at the time the agency assumed responsibility for the study - to seek the input and recommendations of The American Legion and other veterans organizations, and to maintain open lines of communication. For this we are appreciative.

The only other thing that we can ask is that CDC release all relevant findings as they become available during the studies. Vietnam veterans are concerned about the effects of Agent Orange and other environmental hazards and want the facts as best they can be established. The American Legion's goal is to make absolutely sure that these concerns and apprehensions are promptly and accurately addressed.

Mr. Chairman, we will now offer comment on some of the other Agent Orange related research projects that are currently being

carried out by the Veterans Administration, other Federal agencies, and by private entities under contract to the government. The American Legion is monitoring all of these studies, within the limits of our capabilities, and it is hopeful that the results of each of the projects will complement the total Agent Orange research effort.

The Centers for Disease Control in Atlanta is conducting a study that is designed to determine whether or not veterans who served in Vietnam are at a higher risk of producing offspring with serious birth defects. The test population consists of approximately 7500 babies with birth defects born in the Atlanta area between 1968 and 1980, the identity of which were extracted from the CDC birth defect registry. Where possible, the parents of the subject babies are being interviewed to determine the factors which may be responsible for the occurence of the abnormalities, including service in Vietnam and possible exposure to toxic substances which may be attributable thereto. Reportedly, CDC has experienced a good participation rate in this study. However, we understand there are some problems in locating a small number of veterans who were previously interviewed, and are now being contacted for follow-up interviews, due to the fact they have moved. The results of this study are expected to be available by the end of 1983.

The Armed Forces Institute of Pathology, since 1978, has been collecting pathologic material including tissues extracted during surgical procedures and during autopsy procedures, of

Vietnam veterans from Veterans Administration medical centers, Armed Forces hospitals, and from medical facilities in the private sector, for the purpose of surveying the illnesses that have been incurred by these Vietnam veterans. It was recently reported that 1200 cases have been submitted to AFIP to date, and an additional 600 are forthcoming. The project is being divided into two phases. The first phase is the collection and evaluation of the cases of veterans who served on active duty in Vietnam from 1962 to 1974. The second phase consists of the collection and evaluation of the cases of veterans or active duty personnel who did not serve in Vietnam. This group will served as matched controls for the cohort included in phase one. We find it interesting to note the different diagnoses that have been made thus far. There are 86 different diagnoses of the skin, 15 varied liver diagnoses, 16 different benign tumor diagnoses, and 30 diagnoses of malignant tumors. There have been an additional 173 diagnoses made, not including the foregoing. As for the collection of the pathologic tissue, 1088 samples are submitted by VA medical centers, 74 of the cases involved veterans in civilian hospitals, and the remaining 4 percent were submitted by Federal hospitals, for the most part Air Force. The tissue samples have been sent to AFIP from 46 States, and 99 percent of the cases involved male veterans. The completion date of this study is indefinite.

The Veterans Administration has begun preliminary work on a Vietnam veteran mortality study which will draw a comparison of death rates and the causes of death between groups of veterans who served in Vietnam and those who did not. VA estimates that this

study will be completed in mid-1984.

An identical twin study is currently being designed by the VA at the St. Louis VAMC. The proposed study will compare a significant number of pairs of twins; one of whom served in Vietnam and the other who was in the military but was not in RVN, to examine the effects of the Vietnam experience. This study is expected to be concluded in mid-1984.

Ten additional research projects were approved late last year by the Administrator of Veterans Affairs, selected from proposals submitted by individual investigators working in VA medical centers, in response to a request for new research proposals issued by VA Medical Research Service, which specified a biochemical, physiological or toxicological focus on the delayed effects of exposure to Agent Orange and other herbicides. The research projects for the most part involve animal studies, but human tissue cultures will be analyzed in some of the experiments, such as biochemical studies of fat metabolism. The new projects are supported for up to five years with VA research funds in excess of $2 million.

The VA has established an Environmental Medicine Monograph Series which was designed to provide useful information of a scientific nature on environmental and occupational factors that have or may have affected the health of Vietnam veterans. The Monographs that are to be initiated in Fiscal Year 1983 include Agent Blue (cacodylic acid), Human Exposure to Phenoxy Herbicides, Birth Defects (genetic screening and counseling), and Chloracne. The American Legion will continue to monitor the development of

these and other monographs that have been proposed for future implementation.

The Legion is also following with interest several other ongoing studies involving dioxin exposure, including the National Institute for Occupational Safety and Health (NIOSH) Dioxin Registry, the NIOSH Soft Tissue Sarcoma Investigation, and the National Cancer Institute's Case Control Study of Lymphoma and Soft Tissue Sarcoma.

Our National Commander, Al Keller, Jr., recently announced a joint research effort entitled The Columbia University and American Legion Study of Vietnam Era Veterans, that will commence later this year. It is a broad-based study that will look at a number of problems that are facing Vietnam veterans, including questions surrounding the issue of Agent Orange. The study will use trained individuals drawn from the Legion's volunteer network to collect data from a scientifically selected sample of several thousand Legion members who served in Vietnam and a comparison group of Legionnaires who served in the military elsewhere during the same period of time. The study will be developed and directed by Dr. Jeanne Stellman, Associate Professor of Public Health at Columbia University, and her husband Dr. Steven Stellman, Assistant Vice President for Epidemiology of the American Cancer Society.

The protocol for the study is currently under development, and it will be reviewed by an advisory committee of independent scientific experts to ensure its scientific validity. The advisory committee will also monitor the study and review the final report that is expected in November, 1984.

The American Legion will use the findings of the research in its work on behalf of Vietnam veterans and their families before the Veterans Administration, other government agencies and the Congress.

Mr. Chairman, we have presented this compendium of major Agent Orange and related research projects to demonstrate the magnitude of the total effort being put forth to determine the possible consequences of exposure. Needless to say, the picture is changing and it is apparent to the Legion that progress is being made. As was stated earlier, the Centers for Disease Control has moved quickly on the preliminary implementation of the study mandated by PL 96-151, and the expansion of that study authorized by PL 97-72. The agency has determined the complexities involved in such problematic research, and has moved forward to address the studies. We urge that CDC continue to act in an expeditious but cautious manner as they move forward with the Agent Orange and Vietnam experience studies.

The American Legion realizes that because of the complexities surrounding the issue of dioxin exposure that any one study will not answer all of the questions regarding the health effects of such exposure. We strongly recommend that the results of all research projects be used to compliment the total research effort on this most important issue.

Mr. Chairman, we thank you for inviting The American Legion to participate in today's hearing.

Mr. SCHEUER. General Chesney, we'll hear from you and perhaps you might—perhaps you might want to shed some light on some of the questions that were raised by Mr. Sommer.

General CHESNEY. I have not seen the films, of course, that he's seen. Much of this film—I haven't seen the films that he's talking about. Much of this film probably was taken before 1965, when there was some change in the way the Ranch Hands flew.

I would like to ask one of the members that are with me, Mr. Jack Spey, to discuss this. Jack served many tours in Vietnam, has 3½ years in Vietnam, and 7 years with the spray outfit.

Jack.

Major SPEY. Mr. Chairman, my name is Jack Spey. I'm here with General Chesney. I'm president of the Ranch Hand Vietnam Association, which is a group of—veterans group made up of Ranch Hand veterans and I have been president for the past 7 years.

I'll be happy to answer any operational questions concerning the way the unit flew and the committee might desire to ask.

Mr. MCGRATH. Not to belabor the point, but could you react to the assertions that Mr. Sommer has made that there were—by evidence of a film which he saw—that the formations which were flown by those——

Major SPEY. OK; let me—it will take considerable time, but if I may. Our contact with herbicides in Vietnam was on a daily occupational basis. Our job not only included the spraying of the herbicide; it also included the maintenance to the aircraft, the loading of the herbicides, the transferring of the herbicides from 55-gallon drums to their transfer tanks; loading the tanks in the aircraft as well.

In addition, the men were working on the aircraft; the aircraft contained a sizable amount of spillage. We tried not to spill the material because it was $11 a gallon. You don't waste material that is $11 a gallon. It was present, however, on the spray tank in the airplane——

Mr. MCGRATH. Excuse me, is your assertion, then——

Major SPEY [continuing]. Cargo compartment of the aircraft.

Mr. MCGRATH [continuing]. That the exposure—that the Ranch Hand exposure to the agent orange was significant enough in not only the spraying but the handling and the loading—to——

Major SPEY. Sir, if we were to take time to develop a model right here and call this a flight line and go—walk through the steps, I think it would become very evident to anyone in this room that our contact was total, daily—when you'd walk, you'd touch the tank and the material was on your hand.

Mr. SCHEUER. Mr. Sommer mentioned that the men came back drenched in it.

Major SPEY. Sir, on occasion, if we put—if we took battle damage in the cargo department—one of the high-pressure hoses were ruptured, which was not a daily occurrence, but our airplanes absorbed 8,000 enemy rounds in the history of the unit. One airplane has 600 rounds—absorbed 600, and it's currently in the Air Force Museum.

It was not unusual for these pressure lines to be ruptured. If that were to occur, before the flight engineer could shut the pump down, the material, by wind flow, would fly throughout the cargo

department, up through the open side windows where the flight crew was. These windows were flown open, primarily—two reasons: First, it was very hot in Vietnam and we were nonpressurized and nonair-conditioned. Second, it was SOP to have those windows open in case the window would be shattered by a bullet, thereby eliminating fragmentation damage; hopefully the bullet would just come in the empty window and keep right on going.

You know, it's very—the airflow simply flowed through the open cargo doors in the back of the aircraft, which were open to permit the flight engineer to throw smoke in the event of ground fire and flowed forward and out the side cockpit windows.

In speaking to the formation flying, the airplanes normally flew side-by-side, staggered; that's true. However, it was not unusual for the lead aircraft, or the aircraft behind the lead aircraft, to slide in behind the aircraft in front of us, and at which time your windshield just went completely obscured and this occurred often enough that in 1968, they installed a window-washing system, similar to your automobile, where before we had no choice. We were out of the formation. We broke off and went high and dry because we couldn't see any longer except out the side windows.

So we did not make a habit of flying directly behind the airplane in front of us because that wasn't the job. The job was to fly side-by-side, covering the largest area possible. But it did happen on many, many occasions.

Mr. SCHEUER. All right.

General, perhaps you might want to come back and join us at the table.

Thank you very much.

Would you like to complete your testimony? Have you completed your testimony?

General CHESNEY. I'll submit my testimony for the record, sir. Have I completed?

Mr. SCHEUER. Yes.

[The prepared statement of General Chesney follows:]

DEPARTMENT OF THE AIR FORCE

PRESENTATION TO THE SCIENCE AND TECHNOLOGY COMMITTEE

SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH AND ENVIRONMENT

HOUSE OF REPRESENTATIVES

JULY 28, 1983

SUBJECT: Ranch Hand Mortality Study

STATEMENT OF: Major General Murphy A. Chesney
Deputy Surgeon General
United States Air Force

Not for Publication Until Released by the
Science and Technology Committee, Subcommittee
on Natural Resources, Agriculture Research
and Environment, House of Representatives

MAJOR GENERAL (DR.) MURPHY A. CHESNEY

Major General (Dr.) Murphy A. Chesney is Deputy Surgeon General, Headquarters U.S. Air Force, Washington, D.C.

General Chesney was born November 29, 1927, in Knoxville, Tennessee, and graduated from Central High School near Knoxville in May 1945. He attended the University of Tennessee in Knoxville from September 1945 to March 1947 in an accelerated premedical program and graduated with a bachelor of science degree. He earned his doctor of medicine degree in June 1950 from the University of Tennessee's College of Medicine in Memphis.

In June 1951 he completed his internship at the Scott and White Hospital, Temple, Texas, and entered private practice as a surgeon and general practitioner at the Edgar Renegar Clinic in Levelland, Texas. A year later he moved to Rule, Texas, where he was associated with Dr. Robert E. Colbert in the Rule Clinic. While residing there he was elected president of the Chamber of Commerce.

General Chesney entered the U.S. Air Force in April 1955, attended the basic orientation course at Gunter Air Force Base, Alabama, and later the primary course in aviation medicine at Randolph Air Force Base, Texas. In July 1955 he was assigned to the dispensary at Portland International Airport, first as flight surgeon and then as commander. He continued to serve as commander when the dispensary became a hospital.

From July 1957 to June 1960, General Chesney was at the University of Tennessee in Memphis where he completed his Air Force-sponsored residency in internal medicine. During his last year of residency he was appointed chief resident and was involved in several research papers and projects. He also served as a university instructor from July 1959 to June 1960. For the next two years he was assigned as chief of hospital services and chief of the Department of Internal Medicine at Homestead Air Force Base, Florida.

In May 1962 he transferred to the dispensary at Ben Guerir Air Base, Morocco, as commander. He moved to the 401st Tactical Hospital, Torrejon Air Base, Spain, in June 1963 and became deputy commander and senior internist.

General Chesney returned to the United States in June 1966 and assumed command of the 852nd Medical Group at Castle Air Force Base, California. He became director of professional services in the Office of the Command Surgeon Pacific Air Forces, in August 1969 and deputy command surgeon in June 1972. While there his duties included supervision of the professional medical care of patients, including combat-injured personnel, intratheater aeromedical evacuation, flight medicine, preventive medicine and bioenvironmental engineering, medical aspects of the drug abuse program and the prisoner of war release program.

In April 1973 General Chesney transferred to Headquarters Tactical Air Command, Langley Air Force Base, Virginia, as command surgeon. He moved to Brooks Air Force Base, Texas, in August 1978 where he was commander of the Air Force Medical Service Center. General Chesney served as director of medical plans and resources, Office of the Surgeon General, Headquarters U.S. Air Force, from January 1980 until assuming his present position in April 1980.

General Chesney is a member of the Society of Air Force Physicians, Society of Air Force Flight Surgeons, International Congress of Medical Astronautics and Cosmonautics and Phi Rho Sigma Medical Fraternity. He is a fellow of the American College of Physicians, fellow of the American College of Preventive Medicine and diplomate of the American Board of Internal Medicine.

He holds the aeronautical rating of chief flight surgeon. His military decorations and awards include the Distinguished Service Medal, Legion of Merit, Meritorious Service Medal, Air Force Commendation Medal, Air Force Outstanding Unit Award ribbon, National Defense Service Medal and the Spanish Cross of the Aeromedical Order of Merit, 2nd Class.

He was promoted to major general February 8, 1979, with date of rank July 1, 1975.

General Chesney is married to the former Mary Ann Wilson. They have four children: Murphy A. III, Charles Allen, Carol Jean and John Lowell.

Mr. Chairman and Members of the Committee

I am Major General Murphy A. Chesney, Air Force Deputy Surgeon General. I thank you for the opportunity to present an update on the progress of the Air Force Epidemiologic Study of Ranch Hand personnel exposed to herbicides in Vietnam between 1961-1971. Our previous Congressional presentations have included information on the use of herbicides in Vietnam, the development and peer review process of the Air Force study design and protocol, the process of study implementation, compliance figures, program costs and preliminary mortality findings.

The Air Force has now completed the first mortality report, and I will present the results of this baseline mortality study to you today.

Twelve hundred sixty-nine (1269) individuals who were assigned to Air Force units directly involved in Operation Ranch Hand were identified through extensive searches of military historical and personnel records. These men were generally exposed to herbicides for up to 10-12 hours a day, 5 to 6 days a week, for periods of at least one year. Thus, the Air Force considers them to be the most heavily herbicide exposed group of U.S. military personnel in Vietnam. For the purpose of statistical comparison, a group of other Air Force personnel assigned to duty in Southeast Asia was selected. They were matched to the Ranch Hand group by race, job and date of birth. Five comparison subjects were selected for each of the Ranch Handers to improve the ability of the study to detect a difference in death experience. The death experience of the herbicide/dioxin exposed group was contrasted with the death experience of the matched group, and three other groups external to this study--the 1978 U.S. white male population, a Department of Defense (DOD) retired population, and the 1956 class of West Point.

All Ranch Hand and comparison subjects designated as killed in action (KIA) were removed from the study population, leaving 1247 Ranch Handers and 6171 comparison subjects for the mortality determination. Analysis of these KIA deaths will be performed for the next annual report of mortality. As of December 31, 1982, 50 Ranch Hand and

250 comparison subjects had died (certified on/before April 27, 1983). This represents only 4% of each group. Death certificates were obtained on all 300 deceased subjects.

Of these 50 Ranch Hand deaths, there were 19-accidental deaths; 3-suicides; 2-homicides; 4-malignant neoplasms; 1-endocrine, nutritional, metabolic and immunity disorder; 16-diseases of the circulatory system; and 5-diseases of the digestive system. For the same time period, there were 250 deaths among the comparison subjects. The larger number of comparison subject deaths is a result of the 1:5 Ranch Hand to comparison subject mortality study design. The causes of death for this group include: 92-accidental deaths; 14-suicides; 3-homicides; 39-malignant neoplasms; 2-neoplasms of uncertain behavior; 1-endocrine, nutritional, metabolic and immunity disorder; 70-diseases of the circulatory system; 11-diseases of the digestive system; 3-infectious and parasitic diseases; 2-nervous system and sense organ disorders; 1-mental disorder; 4-respiratory system diseases; 3-genitourinary system conditions; 2-ill-defined conditions; and 3-unknown conditions. No statistically significant differences in the crude death rates were found between the Ranch Hand and the comparison group. There were no soft tissue sarcoma deaths diagnosed in either group.

Analysis showed that, to date, the mortality experience of the Ranch Hand group is identical to that of the matched comparison group. The overall rates and causes of death are not significantly different between the groups. However, it does appear that officers are living longer than enlisted personnel in both groups. The Ranch Handers did show a relative decrease in cancer, but an increase in liver disorder deaths; however, both of these findings are statistically nonsignificant. The sites of all cancers are shown in the following table:

SITE SPECIFIC MALIGNANT NEOPLASM MORTALITY

	Deaths	
Site ICD Code (9th Ed)	Ranch Hand	Comparison
Lip, oral cavity, Pharynx (140-149)	0	4
Digestive organs, peritoneum (150-159)	0	8
Respiratory, intrathoracic (160-165)	2	15
Bone, connective tissue, skin, breast (170-175)	0	1
Genitourinary organs (179-189)	1	3
Brain (191-192)	0	3
Lymphatic and hematopoietic tissue (200-208)	0	4
No site specification (199)	1	1
	4	39

These data are not adjusted for other medical or environmental risk factors of interest, such as length of time in Vietnam or Southeast Asia, herbicide dose, time since exposure, time in active duty military, or other nonmilitary chemical exposures. The number of cancers is small but, the morbidity data we hope to release in October will include cured cancer cases, ongoing cancer cases, and recorded cancer deaths. These data may be substantially larger and will undergo more refined analysis.

The next table presents the digestive system mortality:

DIGESTIVE SYSTEM MORTALITY

	Deaths	
ICD Code (9th Ed)	Ranch Hand	Comparison
Pancreatitis (5770)	1	2
Alcoholic cirrhosis (5712)	0	3
Nonalcoholic cirrhosis (5715)	3	3
Nonalcoholic fatty liver (5718)	0	1
Chronic liver disease (5728)	0	1
Alcoholic liver disease (5711)	1	0
Duodenal ulcer (5325)	0	1
	5	11

While these findings are preliminary and statistically nonsignificant at this time, they represent a key area of interest for continued analysis.

Analysis of both the overall Ranch Hand and the overall comparison groups to the 1978 U.S. white male mortality experience showed highly significant findings of less mortality than for equivalently aged U.S. white males. Most of these differences can be attributed to the healthy worker effect. This is due to the fact that individuals must be in basically good health upon entry into military service, while the general U.S. population is not subject to this form of "selection." The DOD retired and West Point data were used for further analyses in an attempt to better define the healthy worker effect. The contrast with the DOD data again demonstrated significantly less mortality for Ranch Hand officers, comparison officers and comparison enlisted men. The Ranch Hand enlisted group did have a favorable mortality experience, but not to a statistically significant degree. The reason(s) for these observations are speculative at present, but may include the related factors of sample size, socioeconomic differences, access to medical care, and health education and possible herbicide effects. The West Point

comparison had to be restricted to an analysis of the officer groups since all West Point graduates became officers. This analysis revealed no significant differences in mortality.

In the basic analysis using the matched comparison group, a relative risk of 0.964 was found. Relative risk is the ratio of probability of death in one group (Ranch Hand) to the probability of death in another (matched comparison). If the likelihood of deaths was the same in both groups, the result would be 1; increased mortality in the Ranch Handers would result in a value greater than 1. These findings, therefore, indicated overall equivalence between Ranch Handers and their matched comparisons.

In summary, the mortality analyses described in this report have not revealed any adverse death experience in the herbicide/dioxin exposed group. The results of the analyses, regardless of the source of the comparison data, were consistent. At this time, there is no indication that Operation Ranch Hand personnel have experienced any increased mortality or any unusual patterns of death in time or by cause. They are not dying in increased numbers, at earlier ages, or by unexpected causes. However, the fact that adverse effects have not yet been detected does not imply that an effect may not become manifest at a future time. For this reason, further anlyses are intended, and mortality in the study population will be ascertained annually for the next 20 years.

The analysis of the data collected during the questionnaire and physical examination phases of the Ranch Hand Study is well underway and proceeding on schedule. The report on this aspect of the study will be reviewed by the Advisory Committee on Special Studies Related to the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants. We anticipate that the report will be made available to the public in October.

I will be happy to answer questions at this time.

General CHESNEY. Yes.

Mr. SCHEUER. OK. Mr. Lewis Milford.

Mr. MILFORD. Good afternoon, Chairman. My name is Lewis Milford. I'm a lawyer with the National Veterans Law Center here in Washington, which is a public interest law firm that represents veterans on a variety of issues, including agent orange.

I'm also on the faculty of the law school at American University here in Washington, where I direct the clinical program and also teach a course in toxic substances litigation.

I'd like to limit my remarks to the occurrences of Vietnam veterans and their problems with agent orange, and in particular, the concerns with the Ranch Hand study. I want to address those particularly on two points that have been raised this morning concerning the published concern over dioxin.

I think they're important because I believe the agent orange studies that are done with Vietnam veterans will increasingly play an important role in the public debate over the dangers of dioxins, so it is important to understand what those studies are about, both in terms of their interpretation and I'd like to just finally say something about the issue of causation, which has caused a lot of concern this morning.

For the last 5 years, Vietnam veterans have been victims of a rather sorry spectacle. They have made legitimate and sincere complaints about agent orange and its dioxin contaminant. Generally, they have been dismissed by the Government as essentially emotional reactions. In some cases, in some corners, they—these people, these veterans, have been labeled even "goldbrickers."

Now, in addition to these rather derogatory remarks, the Government has also fought these claims with its own scientific efforts. As you probably know, the major studies, at least numerically, the number of studies that are now being done on agent orange are being done by either the Veterans' Administration or the Department of Defense, agencies which, in the opinion of many veterans I represent, have a clear, if—apparent, if not a real conflict of interest on this issue.

Indeed, until a few months ago, these two agencies had a virtual scientific monopoly on the study of agent orange and its health effects and I think it's important to realize where these studies are coming from. In fact, there was almost a sort of a cottage industry within these agencies to generate information to show how the recent health effects on dioxin were, in fact, less than what one would expect.

I think this is critical, also, because the Government has made it clear that claims on dioxin-connected effects, particularly concerning veterans, will generally be based on these Government studies and that in many cases, studies done outside the Government seem to have much little—very little weight.

As to the Air Force study, in one of those forgotten and rather inconvenient predictions, the National Academy of Sciences 3 years ago reviewed the protocol that was the design for the Air Force study and in that review of the protocol, the National Academy of Science said that it would be very unlikely that the Air Force study would produce any health effects which show the incidence

of any health effects because of the very small sample size, a point that was mentioned this morning.

In fact, the National Academy of Sciences seem to recommend against doing the study. What happened? The study found nothing.

Was it explained, though, that the nothing found was the result of the design of the study, that is, that the study had inherent limitations that likely would find nothing? No, that was not what was said.

Unfortunately, even the principal scientific adviser to the VA, himself an Air Force officer, heralded the results in the next day's Washington Post as good news for the American public. I think that is a disservice in the interpretation of this study.

By the way, the National Academy of Sciences also recommended against the Air Force conducting this study because of the obvious problems of credibility and then again predicted, in fact, the result that occurred, and that is, you have a study that at best has equivocal results and the public simply will not believe an agency that is studying itself, particularly when the results are uncertain or equivocal, as they have been. What happened, nevertheless, the results have been interpreted as they are.

I want to—I want to just make one point on the issue of causation because there's—the notion in the discussion this morning somehow was that causation exists as some magical standard, that there will be a point, and there is a point where it will be easy to determine causation and that it will be a scientific determination about cause and effect.

I would submit that that is—that is the issue of causation—is entirely a matter of social policy and that it is not for the scientists to decide, it is for the legislators and the people to decide what the issue of cause and effect is.

In fact, in the law in cases involving toxic substances litigation, it is very clear that statistical associations are essentially the equivalent of causation and any court of law, statistical associations involving an epidemiological study for the most part will constitute causation for purposes of a jury award of relationship between a chemical and an effect.

I think it's important to realize that there are precedents in this in other areas.

I just want to close by saying, I think it's important that—that studies like the NIOSH study are funded and are funded more so that we have good health studies by independent public health agencies.

Thank you.

[The prepared statement of Mr. Milford follows:]

32-911 O—84——12

NATIONAL VETERANS LAW CENTER
PRACTICING LAW CENTER BUILDING
4400 MASSACHUSETTS AVENUE NW
WASHINGTON, DC 20016
(202) 686-2741

TESTIMONY OF LEWIS M. MILFORD
OF THE
NATIONAL VETERANS LAW CENTER

BEFORE THE
SCIENCE AND TECHNOLOGY COMMITTEE
SUBCOMMITTEE ON NATURAL RESOURCES, AGRICULTURE RESEARCH
AND ENVIRONMENT

UNITED STATES HOUSE OF REPRESENTATIVES

JULY 28, 1983

The American University Washington College of Law

MR. CHAIRMAN AND MEMBERS OF THE SUBCOMMITTEE:

My name is Lewis M. Milford. I am a lawyer with the National Veterans Law Center in Washington, D.C. I am also on the faculty of the Washington College of Law, American University, where I direct a law clinic and teach a seminar in toxic substances litigation. The Center is a public interest law firm which represents veterans in federal court litigation and in federal administrative hearings. The Center has been involved in the controversy over Agent Orange since 1978.

Thank you for the opportunity to present my views on the dioxin controversy, particularly as it involves Vietnam veterans. I have this brief statement and I would be pleased to answer questions.

As a lawyer for the National Veterans Law Center (NVLC), I now represent Vietnam veterans who are concerned about the government's policy on Agent Orange. They are deeply distressed about the government's handling of the matter. As a law school teacher of a seminar on occupational disease litigation, I also am disturbed about the failure of the government to make intelligent health care and compensation policy. The Veterans Administration, the agency responsible for making policy on Agent Orange matters, has made every effort to minimize or dismiss available scientific evidence on the dangers of dioxin. At the same time, it has relied almost exclusively on the scientific advice of the Defense Department for guidance in the Agent Orange controversy.

That reliance gets me to the point of my remarks, the Air

Force Ranch Hand report. I would like to discuss briefly the problems with the report; not as a scientist but as a lawyer for veterans who wants fair, objective public health studies to form the basis for government action. I want also to stress the urgent need for scientific investigations of dioxin's possible health effects conducted by governmental or private institutions that are not compromised by real or apparent conflicts of interest. The investigations now under way by the Defense Department and the VA, which numerically at least appear to constitute the bulk of the government's study efforts, are irrevocably tainted by such conflicts.

When the Air Force announced the results of the mortality phase of its Ranch Hand report mid-day Friday at the beginning of the Fourth of July holiday weekend, they were welcomed as good news by the press and the public. They were interpreted as a sign that Agent Orange may not be as dangerous as some believed. Virtually no attention was paid to the fact that an eminent scientific panel of the National Academy of Sciences three years earlier stated that the Ranch Hand study would most likely find no excess mortality or morbidity. The reason was simple -- not enough people are in the study group to make any valid, statistical conclusions about what would be found. In other words, if nothing is found, then it means nothing, a phenomenon called a false negative. A negative finding is as reassuring as looking at ten people in a large neighborhood to determine if there is an increased rate of some disease in a large metropolitan area. No one would expect to find any

occurrences of rare diseases or death in such a small sample.

Nevertheless, the chief scientific advisor of the VA hailed the results as "good news" in the following day's edition of the Washington Post. Why was it good news? Because the study found nothing wrong, or because the study could be sold to the American public as having found nothing wrong? The American public and Vietnam veterans, in particular, were supposed to be reassured that Agent Orange had caused no fatalities; but the lack of public credibility of these insignificant data was precisely the reason that the same NAS panel recommended three years ago against having the Air Force study its own chemical warfare operation in Vietnam. The panel predicted that false negatives would be used by the government as evidence of no effect. This is precisely what has happened with the report.

Unfortunately, Vietnam veterans are left to sort out the meaning and direction of scientific studies conducted by agencies that have a clear political stake in their outcome. Science for Vietnam veterans means VA or Defense Department science. Only after four years of intense political pressure did the VA turn over to the Centers for Disease Control the conduct of the congressionally mandated epidemiological study of Agent Orange. More outside scientific inquiry is essential both for Vietnam veterans and the American public. We should try to save the public the same turmoil that has plagued veterans' efforts to get to the bottom of the dioxin issue. The public has an important stake in seeing that impartial scientific studies are done on an issue as important as dioxin. They can help

Vietnam veterans by demanding that these studies be done quickly, with public participation and by respectable scientific institutions that are untainted by any suggestion of a conflict of interest.

We welcome the important work of the National Institute for Occupational Safety and Health (NIOSH) studies on the death rate of workers in dioxin industries. Vietnam veterans and their families need work done by disinterested public health professionals in NIOSH. Apparently, NIOSH has not yet decided whether to do more than its current mortality studies. We strongly urge the agency to do more studies on the morbidity and reproductive health of these workers. What we believe is that the most extensive dioxin study now underway, the CDC Agent Orange effort, will take several years to complete and it should not be the principal governmental study on the health effects of dioxin. More work certainly is needed.

Mr. SCHEUER. Mr. Milford, can you tell us something—as a lawyer has something to do with those statistics, what your view is of the statistics we ran into on the NIOSH study where we——

Mr. MILFORD. Mr. Chairman, I must say I'm not a scientist. Statistics certainly isn't my field, but in a—where you have a situation where the incidence of disease is three-, four-, fivefold, manyfold over——

Mr. SCHEUER. Fiftyfold in this case.

Mr. MILFORD. Fiftyfold in this case—over and above——

Mr. SCHEUER. But from an admittedly, comparatively small number of cases.

Mr. MILFORD. Over and above what an expected value would be, that that would be extremely—certainly as a statistical association, I think there's been admission by everyone this morning that that constitutes a statistical association. The question is, What weight do you give to the statistical association?

In a lawsuit—I think as a matter of social policy—that's a question of policy. What weight do you give to that association? A scientist can tell you to do more because the area inevitably is uncertain. That's the nature of the scientific inquiry.

The way to resolve that is through a political or a social decision about how to view that science and that is up to this body, and as was mentioned earlier, the Veterans' Affairs Committee voted to—and establish that there is a connection between soft tissue sarcoma and agent orange exposure.

Mr. SCHEUER. Congressman MacKay.

Mr. MACKAY. Mr. Milford, you're not saying that we should not continue the strongest possible effort to establish a statistical connection, are you?

Mr. MILFORD. No; I'm not saying that at all, Congressman. What I'm saying is that everything—that we should do all we can to learn all we can about the health effects of dioxin exposure, but on the other hand, we have to recognize that there is, and will continue to be, a great deal of uncertainty, simply by the nature of the science of inquiry, there will be uncertainty and there will unlikely be any conclusive finding at any time in the future and the Government—HHS, in fact—said this in the agent orange controversy, that at some point the decision will have to be made, which will be a social decision about questions of compensation or prevention or prohibition of the manufacture of certain chemicals.

But I certainly am not saying that we should not continue to study. What I am saying is that we shouldn't continue to study as an excuse not to make social decisions when they're appropriate.

Mr. MACKAY. It appears to me that we may well have standards set more quickly by the judiciary than we will have them set by the legislative branch just because of suits which are gaining access to information that has not apparently been available otherwise.

It seems to me that's appropriate. In other words, we may find that there is more information that can be obtained through the suits regardless of the outcome.

Mr. MILFORD. I think it's a perfectly appropriate role of private litigation to spur on public action in that I think what we have found in product liability litigation is just that, that those actions serve as the—with real compulsory process—can gain information that would not otherwise be available and that in turn could serve as the basis for informed public health decisions.

Mr. MACKAY. Mr. Sommer, in your written testimony, I think it was yours or perhaps Mr. Egan's, about the joint funding project between American Legion and Columbia University. I'm very interested in that. It appears you're trying to establish a broader statistical base. Is that the purpose?

Mr. SOMMER. Yes, sir, uh, let me clarify one matter. It's not funded by the American Legion and Columbia; it's funded by the American Legion and being directed by Columbia.

Mr. MACKAY. Sorry about that.

Mr. SOMMER. It is a broad-based study. It's looking at many problems that face Vietnam veterans, not only the issue of agent orange, but also problems like posttraumatic stress disorder, socioeconomic problems that have faced the Vietnam veterans since their return from the service, and also taking a look at the general health of the veterans who served in Vietnam versus those who served during the same time period but elsewhere in the Nation or the world, and the health of their children on a comparative basis.

Mr. MACKAY. What is the timeframe of that study?

Mr. SOMMER. We expect that the final results will be released in November of next year, so it'll be a total of 18 months. The protocol is under development at this time and we expect to do some pretesting in, hopefully, October of this year.

Mr. MACKAY. Thank you.

Thank you, Mr. Chairman.

Mr. SCHEUER. General Chesney, based on the first results of the Ranch Hand study, is it the position of the Air Force that dioxin does not cause cancer or other diseases resulting in death?

General CHESNEY. No, sir, it is not the position of the Air Force.

Mr. SCHEUER. What isn't? What is your position?

General CHESNEY. We've only made one conclusion so far from our Ranch Hand study, and that is that our ranch handers are not dying off at an unusual rate or for any—or from any unusual problems.

Mr. SCHEUER. Or from any unusual problems.

General CHESNEY. Yes, sir.

Mr. SCHEUER. Enlisted men in the Ranch Hand study seem to be dying off at a faster rate than the officers. What is the significance of this finding?

General CHESNEY. We don't know the significance of this finding at this time. It may be the enlisted men were more heavily exposed and will show an increased death rate in the future. However, in all past studies that we could find where enlisted men and officers were compared as to death rate, the enlisted men always had a higher death rate than officers.

Mr. SCHEUER. And what do you attribute that to?

General CHESNEY. We think that is due to occupational problems. It may be lifestyle, alcohol, cigarettes, that sort of thing.

Mr. SCHEUER. The Ranch Hand study shows a fivefold increase in deaths among Ranch Hand participants from liver disorders, five times more than would be expected in the general population. How do you interpret this finding?

General CHESNEY. No; it's five times more than the controls that we matched them against.

Mr. SCHEUER. Right.

General CHESNEY. This, again, may be evidence of early liver disease that we're seeing in the study. It may be a statistical chance aberration. We don't know. We're going to have to look further into these liver deaths and see what we can come from it.

Mr. SCHEUER. You heard Dr. Selikoff testify this morning that by studying the most exposed individuals, those with the most intense and long-term exposure, we can answer dioxin—questions about dioxin health effects—in a relatively short time, let's say 3, 4—2, 3 years, perhaps.

Do you concur with this statement, and if you do, will the Air Force follow this approach?

General CHESNEY. Well, the whole problem is, this is an unknown and we don't know what we're going to find, so I don't necessarily concur with his statement. I think these people should be studied, but I don't know the results that we're going to find.

The Air Force intends to do this study for 20 years.

Mr. SCHEUER. Well, I suppose in terms of our society's knowing more about dioxin and its effects on human health so that we can handle it better in our society, it would be nice—it would be extremely desirable to have results in a much shorter timeframe than that. It would be worth some extra effort and extra expense.

Are you sit back—are you willing to sit back there and just let this rather relaxed scenario play out so that the first important knowledge we get may be 20 years down the pike?

General CHESNEY. Sir, we're going to do it—the mortality study—we've done the mortality study—we're going to update it yearly. The first report on our morbidity or disease report will

come out in October and we're going to update that at 3, 5, 10, 15, and 20 years.

So we're going to continue to follow the ranch hands as closely as we can to find out every bit of disease information, anything else that we can get from these people.

Mr. SCHEUER. Are you familiar with the NIOSH—the first reports of the NIOSH study that we've been hearing about this morning?

General CHESNEY. Yes, sir.

Mr. SCHEUER. Based on that, that there may be a relationship—whether an absolute linear, absolute 100 percent causal relations, we don't know—but that there may be a relationship between dioxin exposure and human health and health death.

Would you, as a medical man, if we had to play it over again in Vietnam or similar scenario someplace else, would you recommend against the use of agent orange in Southeast Asia or any other continent?

General CHESNEY. A few days ago, I said I wouldn't. There's more evidence today than there was a few days ago. John F. Kennedy made the personal decision to use agent orange in Vietnam on the request of the President of South Vietnam.

I would not to try to go back and second-guess that great American.

Mr. SCHEUER. Well, that great American didn't have anywhere nearly the knowledge base that you have today——

General CHESNEY. Yes, sir.

Mr. SCHEUER [continuing]. As to the lethal effects of agent orange on people that can come into contact with it. Maybe he would have made a different——

General CHESNEY. He probably would've.

Mr. SCHEUER [continuing]. Decision. So looking at it from hindsight—being a 20—being a Monday morning quarterback is always a great, great advantage, and we're giving you that opportunity that President Kennedy never had.

Now, looking at it from the hindsight of history, looking at it from the evidence that you've learned today that you didn't have only a few days ago, how would you call it?

General CHESNEY. I would probably still use it and still say that it saved thousands of lives in Vietnam.

Mr. SCHEUER. All right. You've all been very patient. It's exactly 1 o'clock and you've sat here for many hours and we thank you all for your fine testimony. There will be some additional questions that will follow by mail.

We appreciate your testimony. Thank you.

The meeting is adjourned.

[Whereupon, at 1 p.m., the subcommittee was adjourned, to reconvene, subject to the call of the Chair.]

APPENDIX

ADDITIONAL MATERIAL SUBMITTED FOR THE RECORD

PROJECT RANCH HAND II

AN EPIDEMIOLOGIC INVESTIGATION OF HEALTH EFFECTS IN AIR FORCE PERSONNEL FOLLOWING EXPOSURE TO HERBICIDES

BASELINE MORTALITY STUDY RESULTS

30 JUNE 1983

Prepared for:
The Surgeon General
United States Air Force
Washington, D.C. 20314

Approved for public release; distribution unlimited

EPIDEMIOLOGY DIVISION
DATA SCIENCES DIVISION
USAF SCHOOL OF AEROSPACE MEDICINE (AFSC)
BROOKS AIR FORCE BASE, TEXAS 78235

Unclassified
SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) AN EPIDEMIOLOGIC INVESTIGATION OF HEALTH EFFECTS IN AIR FORCE PERSONNEL FOLLOWING EXPOSURE TO HERBICIDES: BASELINE MORTALITY STUDY RESULTS		5. TYPE OF REPORT & PERIOD COVERED Annual Report, Initial Report 6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) George D. Lathrop, Colonel, USAF, MC; Patricia M. Moynahan, Colonel, USAF, NC; Richard A. Albanese, M.D.; William H. Wolfe, Lt Colonel, USAF, MC		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS USAF School of Aerospace Medicine (EK) Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas 78235		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
11. CONTROLLING OFFICE NAME AND ADDRESS The Surgeon General United States Air Force Washington, D.C. 20314		12. REPORT DATE 30 June 1983 13. NUMBER OF PAGES 61
14. MONITORING AGENCY NAME & ADDRESS(If different from Controlling Office)		15. SECURITY CLASS. (of this report) Unclassified 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE
16. DISTRIBUTION STATEMENT (of this Report) Approved for public release; distribution unlimited.		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)		
18. SUPPLEMENTARY NOTES		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) Epidemiologic investigation Air Force Health Study RANCH HAND Matched cohort design Nonconcurrent prospective design Mortality study		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) In 1979 the United States Air Force (USAF) made the commitment to Congress and to the White House to conduct an epidemiologic study of the possible health effects from chemical exposure in Air Force personnel who conducted aerial herbicide dissemination missions in Vietnam (Operation RANCH HAND). The purpose of this epidemiologic investigation is to determine whether long-term health effects exist and can be attributed to occupational exposure to herbicides. This study uses a matched cohort design in a nonconcurrent prospective setting, incorporating mortality, morbidity, and follow-up studies.		

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

Unclassified
SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

Unclassified
SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

The purpose of this report is to present the baseline mortality study results. As of December 31, 1982, 50 Ranch Hand and 250 comparison subjects had died (certified on/before April 27, 1983). Data analysis showed that the mortality experience of the Ranch Hand group is nearly identical to that of this comparison group. However, this mortality report can in no way be regarded as conclusively negative since the study population may not yet have reached the latency period. Subsequent mortality reports will include additional anaylses and will be updated annually for the next 20 years.

Unclassified
SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered)

EXECUTIVE SUMMARY
Baseline Mortality Study

The Ranch Hand II epidemiologic study uses a matched cohort design in a nonconcurrent prospective setting, incorporating mortality, morbidity, and follow-up studies. The purpose of this report is to present the baseline mortality study results.

Since 1979, a detailed population ascertainment process has enumerated a total of 1269 Ranch Hand personnel who served in Vietnam during the period of 1962-1971. As described in the protocol, this total is believed to comprise the entire exposed study population. The eligibility of each Ranch Hander was verified by a hand review of his personnel record. A comparison group was formed by identifying all individuals assigned to selected Air Force organizational units with a mission of flying cargo to, from, and in Vietnam during the same period. All Ranch Hand and comparison subjects designated as killed in action were removed from the study population. By a computerized nearest neighbor selection process, up to 10 comparison individuals were matched to each Ranch Hander by job category, race, and age to the closest month of birth. A hand record review of the matched comparison sets revealed that on the average, 8.2 comparison individuals were fully suitable for study. From each matched comparison set, five individuals were randomly selected for the mortality study, yielding a 1:5 design. Every Ranch Hander and his set of comparisons will be the subjects of annual mortality updates throughout the entire 20 years of the follow-up study so that emerging mortality patterns or disease clusters may be detected with maximal sensitivity. Each living Ranch Hander and his first and willing comparison match were selected to participate in a comprehensive physical examination and an in-home interview; the results of this study will be presented in a subsequent report in late 1983.

A mortality determination on 1,247 Ranch Handers and 6,171 comparison subjects was made, sequentially using the data sources of the Air Force, Veterans Administration, Social Security Administration, Internal Revenue Service, and personal contact efforts. As of December 31, 1982, 50 Ranch Hand and 250 comparison subjects had died (certified on/before April 27, 1983). Death certificates were obtained on all 300 deceased subjects and were coded by an Air Force nosologist (ICD, 9th ED). All codings were verified by the National Center for Health Statistics. Autopsy results are currently being sought for future analyses.

Statistical analyses of noncause specific death emphasized survival curve estimates, linear rank procedures, relative risk estimates, and standardized mortality ratios (SMRs). Cause specific analyses were limited to relative risk estimates because of small cell sizes. In addition to these approaches, three other data bases were contrasted to the Ranch Hand population, where possible; the 1978 US White Male Mortality experience, the 1978 Department of Defense (DoD) Nondisability Retired Life Table, and the mortality experience of the West Point Class of 1956. These additional comparison groups have substantial comparability or sample size limitations, rendering conclusions to the weakest order. Analyses with these "external" comparison groups were accomplished to crudely define the healthy worker effect and to determine if the Ranch Hand group mortality was drastically out of line with that of other military populations.

Data analysis showed that the mortality experience of the Ranch Hand group is nearly identical to that of the comparison group. Analyses showed that officers are living longer than enlisted personnel in both Ranch Hand and comparison groups. This difference between officers and enlisted personnel was statistically significant in the comparison group whereas it was not in the Ranch Hand cohort. A contrast of the Ranch Hand and comparison group to the 1978 DoD Life Table showed significantly less mortality for Ranch Hand officers, comparison officers and comparison enlisted men, however, there was not a statistically significant favorable mortality rate for Ranch Hand enlisted personnel. This pattern of mortality was also seen in a contrast of the Ranch Hand and comparison groups to the 1978 U.S. white male mortality experience. That is, highly favorable mortality differentials for Ranch Hand officers, comparison officers and comparison enlisted personnel were observed, but not for Ranch Hand enlisted. This trend is consistent with the self perceptions of differential herbicide exposures reported by many of the Ranch Hand subjects. The reason(s) for these observations are speculative at present, but may include the related items of sample size, socioeconomic differences, access to medical care, and health education and possible herbicide effects. Cause specific analyses were statistically nonsignificant. The Ranch Handers showed a relative paucity of overall cancer but an excess of digestive disorder deaths, both statistically nonsignificant. No soft tissue sarcoma deaths were detected in either group. Analyses of both the Ranch Hand and the comparison groups to the 1978 US white male mortality experience showed highly significant favorable findings. Most of these differences are speculatively attributed to the healthy worker effect. A contrast of the Ranch Hand and comparison groups to the 1978 DoD Life Table showed significantly less mortality for Ranch Hand officers and comparison officers and enlisted men. The West Point comparison showed nonsignificant SMRs of 0.530 and 0.778 for the Ranch Hand officers and the comparison group officers, respectively. Overall, the limitations of the statistical power calculations in most of these analyses were substantial in most analyses due to 1) the low mortality rate (4%) in the Ranch Hand and comparison groups to date, 2) the inherently small group of Ranch Handers (as described in the study protocol), and 3) the observed relative risks which approached unity in most categories.

This baseline mortality report can in no way be regarded as conclusively negative because this small, young, and relatively healthy cohort may not have yet reached the latency period wherein attributable fatal disease might be expected and detected within limited power boundaries of this study. Future commitments for the annual mortality updates include detailed covariate analyses for disease risk factors, herbicide exposure, and confounding industrial chemical exposures. Further, subsequent morbidity reports will include full spectrum, disease specific analyses, e.g., cancer (fatal, ongoing, cured) in an effort to enhance study sensitivity to emerging herbicide effects, if they occur.

PREFACE

In October 1978, the United States Air Force (USAF) Surgeon General made the commitment to the Congress and to the White House to conduct an epidemiologic study of the possible adverse health effects arising from the herbicide exposure of Air Force personnel who conducted aerial dissemination missions in Vietnam (Operation Ranch Hand). The purpose of this epidemiologic investigation is to determine whether long-term adverse health effects exist and whether they can be attributed to occupational exposure to herbicides and their contaminants. The study protocol (1) for this effort incorporates a matched cohort design placed in a nonconcurrent prospective setting. The study approach includes mortality, morbidity, and follow-up elements linked tightly in time, in order to produce the most data in the shortest period of time. The study addresses the question: Has there been, or are there currently, or will there be any adverse health effects among former Ranch Hand personnel caused by repeated occupational exposure to 2,4,5-T containing herbicides and the contaminant, TCDD? At the request of the Principal Investigators (see Appendix I) the study protocol was extensively and independently peer reviewed. The review agencies included: The University of Texas School of Public Health, Houston Texas; the USAF Scientific Advisory Board; the Armed Forces Epidemiological Board; and the National Research Council of the National Academy of Sciences. In 1980, the Science Panel of the Agent Orange Working Group was created as an additional peer review agency. This group, redesignated as the Advisory Committee on Special Studies Relating to the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants, has consented to the oversight responsibility of the Ranch Hand study and continues to monitor the conduct of this epidemiologic investigation (see Appendix II). The approved and official protocol for this effort is available to the public through the National Technical Information Services, 5285 Port Royal Road, Springfield, Virginia 22161.

The Ranch Hand II Study protocol heralds the suboptimal statistical power of the mortality study. The mortality study was motivated by the desire to use a full spectrum epidemiologic approach to the herbicide question. Additionally, the investigators were scientifically obliged to pursue the mortality study because of previous and emerging studies (some with small sample sizes) which suggested the possibility of a soft tissue sarcoma end point (2,3,4). Within the inherent sample size limitation of the Ranch Hand population, detection of such a rare condition will be missed unless there is marked case clustering and correspondingly high relative risks.

Also, because of sample size limitations as well as the myriad of proposed clinical end points, a case-control design was not entertained. The investigators have attempted to enhance statistical power and analytic sensitivity where possible by using 1) a large comparison group, 2) precise matching procedures, 3) annual mortality updates, 4) mortality-morbidity linkages, 5) a lengthy follow-up study, 6) external comparison groups, and 7) state-of-the-art statistical methodology. A final assessment of overall mortality must necessarily await substantially more data and covariate approaches to identify and isolate unusual emerging mortality patterns, if they occur.

This report is primarily directed to individuals with statistical and epidemiologic backgrounds. It also assumes that the reader has a familiarity with the herbicide/dioxin issue and a detailed knowledge of the protocol of the Air Force study. In the interest of brevity, the reader is referred to the protocol published as US Air Force School of Aerospace Medicine Technical Report 82-44.

32-911 O-84——13

Page

Executive Summary i

Preface iii

Table of Contents v

Chapter I. THE MORTALITY STUDY DESIGN 1

1. The Study Population. 1
2. The Mortality Population. 2

Chapter II. THE MORTALITY DETERMINATION PROCESS 4

1. Introduction. 4
2. United States Air Force Data Sources. 4
3. Veterans Administration Death Beneficiary Identification and Record Location Subsystem. 6
4. Other Governmental Data Sources 6
5. Morbidity Population Tracking 6
6. Receipt and Coding of Death Certificates. 7
7. Results 8

Chapter III. RANCH HAND VERSUS COMPARISON GROUP ANALYSES 9

1. Introduction. 9
2. Overall Comparisons 9
3. Noncause Specific Occupational Comparisons. 15
4. Cause Specific Ranch Hand Versus Comparison Mortality 17

Chapter IV. NONCAUSE SPECIFIC COMPARISONS WITH EXTERNAL POPULATIONS 20

1. Background and Motivation 20
2. Adjustment Difficulties 20
   A. Adjustment for Calendar Year of Death 20
   B. Adjustment for Military Status (Active Duty, Separated, Retired). . 20
   C. Adjustment for Selection. 21
   D. Adjustment for Branch of Service. 21

3. Comparisons with 1978 DoD Life Tables 21
4. Comparisons with U.S. 1978 White Male Life Table. 24

Chapter V. COMPARISONS WITH THE WEST POINT STUDY GROUP 28

1. Background and Motivation 28
2. Noncause Specific Comparisons of Ranch Hand and Comparison Subgroups with the West Point Study Group 28
3. Cause Specific Comparisons. 31

Chapter VI. STATISTICAL ASPECTS 34

1. Purpose 34
2. Survival Curve Estimates and Confidence Bands 34
3. Linear Rank Procedures. 35
4. Relative Risk Estimation. 36
5. Indirect Standardization. 37
6. Comparing Observed Life Table Data with a Known Survival Curve. 37

Chapter VII. CONCLUSION 39

1. Introduction. 39
2. Internal Comparison Group 42
3. External Comparisons. 42
4. Power Considerations. 42
5. Consistency Patterns. 43

APPENDICES

I. Ranch Hand II Principal Investigators, Coinvestigators, Contributors, and Management Personnel. 45
II. Advisory Committee on Special Studies Relating to the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants . . 47
III. Matching Results in the Mortality Population. 48
IV. Year of Birth, Occupational and Race Specific Mortality 51
V. The Extended Ejigou-McHugh Relative Risk Estimator. 53
VI. Survival Curves and Confidence Bands for Ranch Hand and Comparison Subgroups. 54

REFERENCES. 59

Chapter I

THE MORTALITY STUDY DESIGN

1. The Study Population

The exposed study population, termed "Ranch Hand", was defined as those individuals who were formally assigned to the USAF organizations responsible for the aerial dissemination of herbicides and insecticides in the Republic of Vietnam from 1962 to 1971. These individuals were identified from historical data sources at the National Personnel Records Center (NPRC), St. Louis, Missouri and the USAF Human Resources Laboratory, Brooks Air Force Base, Texas. A total of 1,269 Ranch Hand personnel were eventually identified through this process. The comparison population was defined as those individuals who were assigned to a variety of cargo mission organizations throughout Southeast Asia during the same time period. Cargo mission aircrew members and support personnel were selected because of sufficient population size, similar training and military background experiences, and psychologic similarities to the Ranch Hand group. The comparison population was not occupationally exposed to herbicides or insecticides in the Republic of Vietnam. Identification of this population was completed using the same historical data sources as were used with the Ranch Hand population; 24,971 individuals were so identified. In preparation for matching the study and comparison populations, all subjects killed in action (KIA) were removed from the data base. The rationale for this action is the assumption that combat death in the Ranch Hand group was not caused by the immediate effects of herbicide exposure; KIA's were removed from the comparison group for comparability purposes. A KIA analysis will be performed in a subsequent report. The Ranch Hand KIA subgroup, numbering 22 individuals, although not matched, was maintained in the data base but was deleted from the mortality analysis, leaving 1247 Ranch Hand subjects.

The Ranch Hand population was matched to the comparison population with an iterative nearest-neighbor computer program (1). Up to 10 comparison subjects were matched to each Ranch Hander by year of birth, race (Black versus non-Black), and occupational category (officer pilot, navigator and other; enlisted flight engineer and other), thus creating matched sets of one study subject and up to 10 comparison subjects. All subjects are males. The mean age of the study subjects is 45 years.

Following the original match, the majority of Ranch Handers had 10 comparisons. The exceptions were the group of non-Black pilots who had a mean of only 9.5 comparisons per exposed subject due to the extreme ages of several individuals, and the strata of Black pilots and other Black officers who only had means of 2.7 and 5.0, respectively. In December 1981, the USAF Principal Investigators learned that several morbidity study comparison subjects had reported no experience in Southeast Asia, suggesting that overselection of the comparison population had occurred (1). Manual review of the comparison subjects' military personnel records revealed that 18 percent of the 12,193 comparison individuals in the original match were ineligible for study. The inadvertent inclusion of several non-Southeast Asia organizations resulted in the selection of these inappropriate individuals. These ineligible subjects were found to be randomly distributed throughout the matched sets and were removed from the study. Following the removal of the

ineligible subjects, the study was reduced to a 1:8 design. Also during this period, five Ranch Hand subjects were identified through personnel record sources and Veterans Administration Education Benefits and Financial Records. These five individuals had not been identified earlier because the majority of their military personnel records had been destroyed in a fire at the NPRC in St. Louis. Three of these five were newly found Ranch Handers and two were comparisons subsequently identified as Ranch Handers. No attempt was made to match comparisons to these five new Ranch Handers. During the removal of ineligible subjects, one Ranch Hander, a Black officer pilot, lost his only comparison and remains unmatched, giving a total of six unmatched Ranch Handers. All six of these unmatched Ranch Handers are included in the morbidity and mortality studies. They were used in the analyses where appropriate, in order to improve statistical power.

2. The Mortality Population

Five comparisons per exposed subject were considered more than adequate for mortality analyses; this estimate has recently been verified under a multiplicative model by Breslow, et al. (5). Up to five comparisons in each matched set, were identified from the 1:8 cohort as the mortality comparisons. Since the positions of the individuals in the matched sets had already been randomized in the data file, the selection of the first five positions in each matched set array for membership in the mortality comparison resulted in a random selection of the mortality comparison cohort. If a Ranch Hander had at least one but no more than five comparisons after removal of the ineligibles, then all of his matched set were used in the mortality component of this study. The mortality population is, therefore, defined as the 1241 matched Ranch Handers and their randomly chosen mortality comparisons (6171 individuals) and the six unmatched Ranch Handers. Table 1 summarizes the mortality population by occupational category and race. Here, and elsewhere in this report, non-Black is defined as Caucasian, Mexican or Oriental.

Table 1

MORTALITY POPULATION SUMMARY BY OCCUPATION AND RACE

Occupation, Race	Counts	
	Ranch Hand	Comparison
Officer-Pilot, Non-Black	349	1740
Officer-Pilot, Black	6	13
Officer-Navigator, Non-Black	80	390
Officer-Navigator, Black	2	10
Officer-Other, Non-Black	25	123
Officer-Other, Black	1	2
Enlisted-Flt Eng, Non-Black	189	935
Enlisted-Flt Eng, Black	15	75
Enlisted-Other, Non-Black	528	2628
Enlisted-Other, Black	52	255
	1247	6171

The overall match ratio, 6171/1247=4.95, reflects the lack of suitable controls in some strata, the subsequent removal of ineligible comparisons and the addition of five unmatched Ranch Handers. A detailed description of the matching results is given in Appendix III.

Those Ranch Handers having fewer than five matched mortality controls are summarized in Table 2.

Table 2

RANCH HAND SUBJECTS WITH LESS THAN FIVE COMPARISON SUBJECTS

Occupation, Race	Counts		Notes
	Ranch Hand	Comparisons[3]	
Officer-Pilot, Non-Black	1	2	1
	1	3	1
Officer-Pilot, Black	1	0	1
	1	1	1
	2	2	1
	1	3	1
Officer-Navigator, Non-Black	2	0	2
Officer-Other, Non-Black	2	4	1
Officer-Other, Black	1	2	1
Enlisted-Flt Eng, Non-Black	2	0	2
Enlisted-Other, Non-Black	12	4	1
Enlisted-Other, Black	1	0	2
	27		

Note 1. Lack of suitable comparison subject or loss due to ineligibility.
Note 2. New Ranch Hander, no attempt to match.
Note 3. Comparisons per Ranch Hander

Chapter II

THE MORTALITY DETERMINATION PROCESS

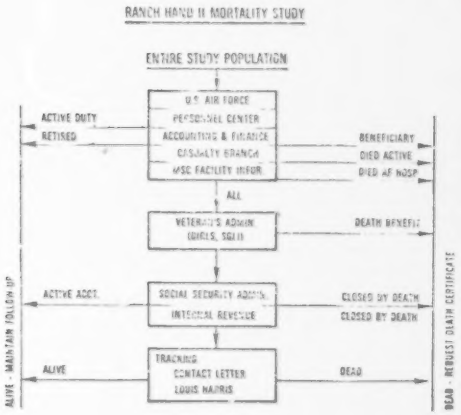
1. Introduction

The mortality status of the Ranch Hand group and their mortality comparisons are, and will continue to be, ascertained using four major data sources: USAF, Veterans Administration (VA), other Governmental and morbidity population tracking. The mortality determination process using these data sources is presented in Figure 1.

Figure 1.

RANCH HAND II

MORTALITY DETERMINATION ALGORITHM



The entire study population was matched or checked against the first three sections of this algorithm while only the morbidity population was contacted and tracked. A description of the data sources within the algorithm follows.

2. United States Air Force Data Sources

The USAF data sources include the USAF Military Personnel Center (MPC) records, the USAF Accounting and Finance Center records, and the USAF Medical

Service Center Facility Use Data. The USAF MPC records include the individual's military personnel record and the data accumulated by the Casualty Branch of the MPC. Individual military personnel records are created at the time of induction into the USAF, and reflect a chronological history of the individual's military career. Epidemiologically, these records are an invaluable data source as they can be used for the development of occupational histories, identification of race, sex, and date of birth as well as for location of personnel, and for determining vital status. Hard copy records of these data are maintained at the individual's base of assignment while on active duty; a computer copy of these records is maintained at the USAF military personnel center, Randolph AFB, Texas. Following retirement and/or separation from the USAF, these records are forwarded to the National Personnel Records Center (NPRC), St Louis, Missouri, the record repository for all military personnel records. They are indexed by Social Security Account Number or Air Force Serial Number at the NPRC. If an individual should die while on active duty, after retirement, or within 120 days of separation from active duty, it is the responsibility of the Casualty Branch of the USAF Military Personnel Center to update the hard copy military personnel record and the MPC computer data base and to inform the USAF Accounting and Finance Center of this fact. At the same time, USAF MPC personnel initiate a copy of the USAF Form 1312, Report of Retired Casualty, or Department of Defense DD Form 1300, Report of Casualty. The selection of the appropriate form is based on the current status of the individual concerned. The DD Form 1300 also clarifies an individual's casualty status which can be either battle or nonbattle. Copies of the appropriate death form are sent to appropriate agencies while the original is placed in the individual's military personnel record.

Since the initial review of military personnel records, a system has been established with the Casualty Branch of the Military Personnel Center wherein all active duty and retired death forms are forwarded monthly to the Occupational Epidemiology Section of the USAF School of Aerospace Medicine Epidemiology Division. In this way, the mortality status of all active duty and retired study subjects is systematically determined on a continuing basis.

The USAF Accounting and Finance Center data base was used as a resource to update individual Air Force serial numbers to Social Security numbers. The Social Security number is required for all other aspects of the mortality algorithm.

The Air Force Medical Service Center (AFMSC) Facility Use Data is a computer data base containing information regarding all active duty and retired deaths that occur in Department of Defense (DOD) Medical Facilities. This data base identified no additional deaths in the mortality population, but did verify the deaths known to have occurred in DOD hospitals.

In addition to the USAF data bases, the Ranch Hand Association, a reunion association of approximately 850 Ranch Handers, has contributed to the success of this study. This group has assisted the Principal Investigators in the ascertainment of the exposed population, and in the determination of the current location and the mortality status of the group. The association contacts all of its members yearly through newsletters and provides updated information to the Air Force investigators.

3. Veterans Administration Death Beneficiary Identification and Record Location Subsystem

The Beneficiary Identification and Record Locator Subsystem (BIRLS) is a Veterans Administration data base generated by the Veterans Administration for determination of funeral allowance. If the family of the deceased informs the funeral director that the deceased served in the US military, the funeral director submits the required data to the Veterans Administration. In January 1981, August 1982,and January 1983,the BIRLS data base was searched for Ranch Hand and comparison deaths. In addition to these searches, the Department for Veterans Benefits, Veterans Administration, coordinated the gathering of death certificates from VA regional offices.

4. Other Governmental Data Sources

A. Internal Revenue Service

Public Law 96-126, Section 502, 28 November 1979, authorized the use of Internal Revenue Service (IRS) addresses for individuals who had been exposed to occupational hazards in order to determine the status of their health. The National Institute for Occupational Safety and Health (NIOSH) coordinated the USAF requests for these IRS addresses. This system is based on the address shown on individual tax returns and is corrected once a year. The addresses are verified by NIOSH through use of a post card mailed to the post office responsible for the individual's mail delivery. NIOSH assumes that the individual is alive if he files a tax return and if the verification scheme confirms his address for mail delivery. The IRS assumes an individual is dead if the individual is so reported on a joint tax return. The IRS data base search provides an incomplete mortality determination, however, since absence of an individual tax return does not necessarily imply death of that individual.

B. Social Security Administration

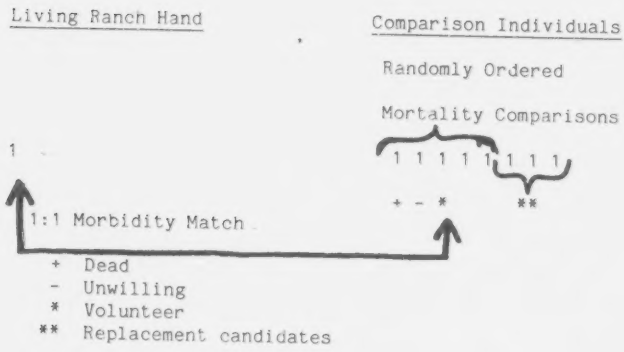
The Social Security Administration (SSA) is a source of mortality information based on data maintained by the Office of Renumeration and Earnings. The basis for this data is employer-reported earnings. The SSA assumes that an individual is living if there is no indication of death on the individuals record and earnings are recorded for the last calendar year or retirement, disability, black lung or supplemental security income payments are being made. The SSA did inform us that they do not conduct an exhaustive search, and all deaths are not necessarily reported to SSA. Therefore, this mortality information may not be complete.

5. Morbidity Population Tracking

Individual tracking techniques apply only to the morbidity population, defined as those selected and compliant to questionnaire. The morbidity population for this effort is defined as all Ranch Handers and their morbidity comparisons. The morbidity comparisons are, in general, also mortality comparisons. The selection procedure for the morbidity study is presented in Figure 2.

Figure 2.

SELECTION PROCEDURE FOR THE QUESTIONNAIRE,
PHYSICAL EXAMINATION, AND FOLLOW-UP STUDY



In this figure, the first randomly ordered comparison was found to be dead. The second was contacted but was unwilling to participate and the third volunteered to participate in the questionnaire component of the morbidity effort. This contacting process for the morbidity effort was the final step in the baseline mortality determination. The original contact was made by certified mail. Each Ranch Hander and a random living comparison were sent an introductory letter and fact sheet signed by the USAF Surgeon General. A Louis Harris and Associates (LHA) interviewer then accomplished an in-home interview.

LHA identified two Ranch Handers and nine comparisons who could not be located. All eleven unlocatable subjects were assumed living and remain included in the mortality study.

6. Receipt and Coding of Death Certificates

Death certificates were ordered from the vital statistics department of the appropriate state, trust territory, or foreign country. Death certificates or their equivalent were obtained on all appropriate subjects.

All death certificates were coded by two individuals, trained by the National Center for Health Statistics (NCHS) in underlying and multiple cause of death coding procedures, using the International Classification of Diseases, Ninth Edition (1977) coding system. Classification of the underlying cause of death was in accordance with NCHS decision tables. Each coder independently classified the underlying and multiple causes of death and gave the coding worksheet, with each corresponding death certificate, to the coding supervisor, a trained nosologist, for reconciliation. Following reconciliation, one of the coders placed the death code information, by computer terminal, in the death certificate mortality file via a blind verification program designed to mimic the NCHS underlying multiple cause of death coding sheet. At the

conclusion of this initial input of the death codes, a copy of the death certificate was forwarded to NCHS for further validation. The NCHS returned coded death certificates, which were then compared with the Air Force classification. Discordances were resolved in cooperation with NCHS and entered into the data base.

7. Results

Chapter II has reviewed the comprehensive, cohesive, sequential ascertainment process of death in the study populations. This process has resulted in the identification of 50 dead Ranch Hand subjects and 250 dead comparison subjects. Although it is understood that early differential ascertainment occurred in the Ranch Hand members (because of detailed knowledge of the study group), it is judged that the overall comprehensive ascertainment process is currently balanced with respect to the two groups.

Table 3 and Appendix IV contain summary counts by age, job, and race category for all Ranch Handers and their mortality comparisons; these counts reflect mortality as of 31 December 1982, as known on 27 April 1983. In the stratified analyses, the term "at risk" is defined as simply the number of subjects within a specific stratum, and in life table analyses, as the number of subjects entering a specific age bracket. The term "rate" is the proportion of those individuals "at risk" who are dead.

Table 3

OCCUPATIONAL AND RACE SPECIFIC MORTALITY

		Ranch Hand			Comparisons		
Race	Occupation	At Risk	Dead	Rate	At Risk	Dead	Rate
Non-Black	Officer-pilot	349	12	.034	1740	72	.041
	Officer-navigator	80	2	.025	390	13	.033
	Officer-other	25	1	.040	123	3	.024
	Enlisted-flt eng	189	6	.032	935	46	.049
	Enlisted-other	528	25	.047	2628	97	.037
Black	Officer-pilot	6	0	.000	13	0	.000
	Officer-navigator	2	0	.000	10	0	.000
	Officer-other	1	0	.000	2	0	.000
	Enlisted-flt eng	15	2	.133	75	9	.120
	Enlisted-other	52	2	.038	255	10	.039
	TOTAL	1247	50	.040	6171	250	.041

Chapter III

RANCH HAND VERSUS COMPARISON GROUP ANALYSES

1. Introduction

Overall survival comparisons, without regard to cause of death, were made via survival curve estimation, linear rank procedures, relative risk estimation and standardized mortality ratios. Survival curves were estimated and plotted using the method of Kaplan and Meier (6); 95% confidence bands (7) for each survival curve estimate were also plotted on each graph. Linear rank testing was carried out using the logrank test and Prentice's censored data extension of the Wilcoxon test (8). All linear rank tests were carried out with matched sets merged when Ranch Hands differed by less than one year relative to date of birth, within each stratum of job and race (9). These merged matched sets were regarded as separate strata for testing purposes (9, 10, 11). Relative risk estimates and confidence intervals were computed using an extension of the method of Ejigou and McHugh (12) to variable length, one-to-many matched sets (see Appendix V). Here, due to the one-to-many limitation of the algorithm, matched sets were not merged as when testing procedures were performed. Standardized mortality ratios and associated tests and plots were carried out as in Gail (13).

These analyses are fully adjusted for the matching variables, age, race and occupation, but are unadjusted for other variables of interest, such as length of time in Vietnam or Southeast Asia, herbicide dose, time since exposure, time in active duty military, and other medical or occupational risk factors. Some of these variables, such as herbicide dose and time since exposure will be adjusted for in the next analyses, after such data become available. In particular, latency analyses cannot be undertaken at this time but will be included in the next mortality report.

In these analyses, we have used summary statistics for which underlying modeling assumptions can be tested. For this reason, we have used the Breslow-Day (13) approach to SMR calculation, rather than the more traditional person-years method. A detailed explanation of this choice is given in Chapter VI.

2. Overall Comparisons

Survival time in these analyses was regarded as independent of censorship, if any, and was taken to be age at death. All subjects not certifiably dead, as of 31 December 1982, at the time of analysis, were considered censored at their age on that date. Contact has been lost with two Ranch Handers and nine comparisons as described in Chapter II, but these are not assumed lost to follow-up for the purpose of mortality determination. They are assumed to have been alive on 31 December 1982. With this assumption, no subjects were lost to mortality follow-up before 31 December 1982 in this study.

Ranch Hand and comparison group survival curve estimates and their associated 95% confidence bands are shown in Figure 3 and Appendix VI for the five groups: pooled, officers, enlisted, flying and ground personnel, as defined in Table 4. The curves for the pooled groups are shown in Figure 3 with the 95% confidence interval bands deleted in the interest of legibility, but they are included in the group specific curves in Appendix VI. Review of

Ranch Hand operations has strongly suggested that Ranch Hand enlisted personnel were more heavily exposed to herbicide than Ranch Hand officers. Further, there is a perception of possible exposure differential between flying and ground Ranch Hand personnel. These notions prompted the above groupings and analyses seen in this and subsequent chapters. Analyses of latency are not possible at this time due to the as yet incomplete nature of the military service data base. These analyses will be performed after the hand review of military tour records has been completed.

Figure 3

SURVIVAL CURVE ESTIMATES FOR POOLED RANCH HANDERS AND COMPARISON SUBJECTS

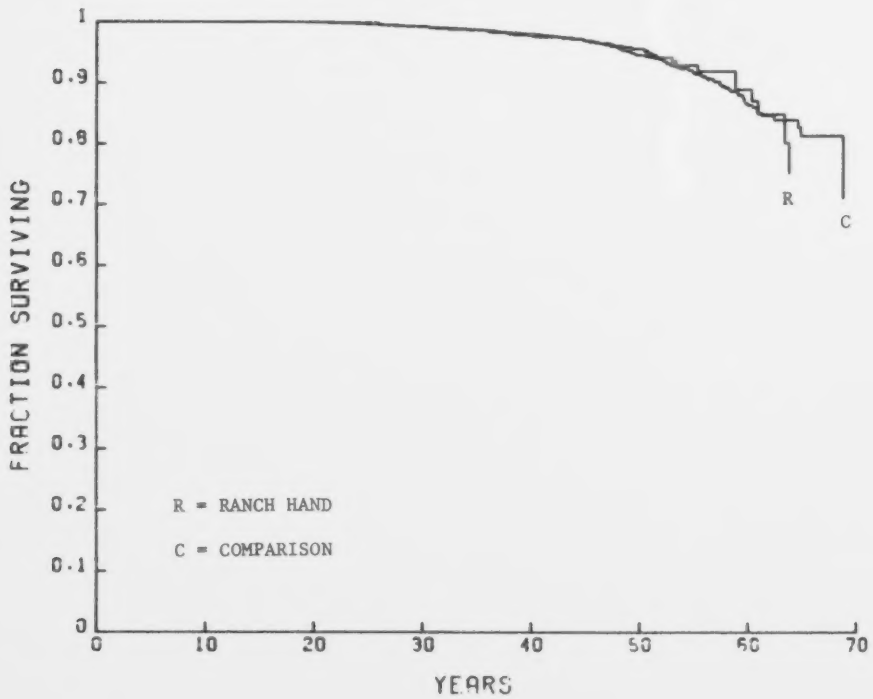


Table 4

GROUP DEFINITIONS

Group	Definition
Officer	Officer-pilot, navigator, other
Enlisted	Enlisted-flight engineer, other
Flying	Officer-pilot, navigator Enlisted-flight engineer
Ground	Officer-other Enlisted-other
Pooled	All occupational categories

Summary counts by group are shown in Table 5. Ignoring the matching, interaction between officer-enlisted categories and Ranch Hand membership, and interaction between flying-ground categories and Ranch Hand membership was evaluated using log-linear models. No statistically significant interactions were detected.

Table 5

SUMMARY COUNTS BY GROUP

	Ranch Hand			Comparisons		
Group	At Risk	Dead	Rate	At Risk	Dead	Rate
Officer	463	15	.032	2278	88	.039
Enlisted	784	35	.045	3893	162	.042
Flying	641	22	.034	3163	140	.044
Ground	606	28	.046	3008	110	.037
Pooled	1247	50	.040	6171	250	.041

Linear rank procedures were carried out on the same five groups. The results, summarized by test statistics and two-sided P-values, are shown in Table 6. Small P-values, less than .05, indicate significant differences, at the 5% level, between the two groups. These procedures are designed so that the statistic will be positive when the Ranch Handers are dying before the comparison subjects and negative when the comparisons are dying prior to the Ranch Handers. The null hypothesis is that the actual survival distributions of Ranch Handers and their matched comparisons are identical. Each statistic is approximately null distributed as a standard normal random deviate.

Table 6

TEST RESULTS AND P-VALUES FOR OVERALL COMPARISONS

Group	Logrank (Value)	Logrank P-Value	Wilcoxon (Value)	Wilcoxon P-Value
Officer	(-0.634)	.526	(-0.722)	.470
Enlisted	(0.383)	.702	(0.331)	.741
Flying	(-1.021)	.307	(-1.116)	.264
Ground	(1.023)	.306	(0.950)	.342
Pooled	(-0.047)	.962	(-0.123)	.902

There is no significant difference, based on these data, between the Ranch Handers and their mortality comparison group. This means that, in particular, the mean ages-at-death of the Ranch Handers and their matched comparisons are not significantly different. In some groups, pooled, officer and flying, the statistics are negative, indicating that the Ranch Handers are living longer than the comparisons, but the differences are, again, insignificant, as evidenced by the large P-values. The situation is reversed for enlisted and ground personnel. These findings are consistent with the observation that, within each group, the comparison confidence bands are contained within the Ranch Hand confidence bands. When matched sets are stratified by five year intervals on year of birth, the same procedures give larger P-values than those in Table 6.

Relative risk estimates, the associated 95% confidence intervals, two-sided P-values for testing the null hypothesis of relative risk equal to unity and the associated power are given in Table 7. Here, the power of the test is defined as the conditional probability of rejecting the null hypothesis at the 5% level of significance, given that the relative risk is equal to its estimated value.

Table 7

RELATIVE RISKS AND 95% CONFIDENCE INTERVALS, P-VALUES AND POWER

Group	Relative Risk	95% Confidence Interval	P-Value	Power
Officer	0.763	(.320 - 1.207)	.373	.105
Enlisted	1.065	(.660 - 1.471)	.742	.072
Flying	0.734	(.387 - 1.081)	.211	.197
Ground	1.232	(.694 - 1.769)	.337	.195
Pooled	0.964	(.658 - 1.269)	.819	.051

The confidence intervals and P-values in Table 7 indicate no significant difference, at the 5% level, between the mortality of the Ranch Handers and comparisons in each of the five groups.

Year-of-birth specific mortality rates for each of the five groups are given in Tables 8 through 12, with the corresponding standardized mortality ratios (SMR). In each group, the comparisons are the internal standard. The SMR estimates relative risk in these comparisons if the year-of-birth specific relative risks are all equal (13). A likelihood ratio test for the hypothesis of equal year-of-birth specific relative risks was carried out for each comparison; its P-value is denoted by P1. In addition, the hypothesis that relative risk is unity, given that relative risk is constant across strata, was tested via a likelihood ratio procedure (13); its P-value is denoted by P2. The SMR and both P-values are given with each comparison.

Here, and elsewhere in this report, the denominator of the SMR is $\sum n_{ij} r_i$, where n_{ij} is the number of individuals for the ith stratum of the jth population and r_i is the death rate, per person, in the standard population for the ith stratum. In these calculations the data is stratified on year of birth.

Table 8

POOLED SPECIFIC MORTALITY RATES BY YEAR OF BIRTH
(SMR = .996; P1=.389, P2=.955)

Birth	Ranch Handers			Comparison		
Year	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-14	5	2	.400	14	2	.143
1915-19	17	4	.235	96	11	.115
1920-24	48	3	.063	241	24	.100
1925-29	84	2	.024	501	40	.080
1930-34	304	15	.049	1389	67	.048
1935-39	207	7	.034	1020	33	.032
1940-44	208	5	.024	1096	23	.021
1945-54	374	12	.032	1814	50	.028
		50			250	

Table 9

OFFICER SPECIFIC MORTALITY RATES BY YEAR OF BIRTH
(SMR = .827; P1=.233, P2=.490)

Birth Year	Ranch Hand Officers			Comparison Officers		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1910-24	41	3	.073	205	17	.083
1925-34	194	4	.021	930	49	.053
1935-39	93	4	.043	458	11	.024
1940-44	90	2	.022	495	6	.012
1945-49	45	2	.044	190	5	.026
		15			88	

Table 10

ENLISTED SPECIFIC MORTALITY RATES BY YEAR OF BIRTH
(SMR = 1.074; P1=.733, P2=.722)

Birth Year	Enlisted Ranch Handers			Enlisted Comparisons		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-14	4	2	.500	12	2	.167
1915-19	9	1	.111	54	7	.130
1920-24	16	3	.188	80	11	.138
1925-29	41	2	.049	211	22	.104
1930-34	153	11	.072	749	36	.048
1935-39	114	3	.026	562	22	.039
1940-44	118	3	.025	601	17	.028
1945-54	329	10	.030	1624	45	.028
		35			162	

Table 11

FLYING SPECIFIC MORTALITY RATES BY YEAR OF BIRTH
(SMR = .769; P1=.678, P2=.238)

Birth Year	Flying Ranch Handers			Flying Comparisons		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1915-24	44	4	.091	220	23	.105
1925-34	272	8	.029	1316	71	.054
1935-39	142	6	.042	698	22	.032
1940-44	120	2	.017	653	14	.021
1945-49	63	2	.032	276	10	.036
		22			140	

32-911 O—84——14

Table 12

GROUND SPECIFIC MORTALITY RATES BY YEAR OF BIRTH
(SMR = 1.257; P1=.535, P2=.302)

Birth Year	Ground Ranch Handers			Ground Comparisons		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-14	5	2	.400	14	2	.143
1915-24	21	3	.143	117	12	.103
1925-29	31	2	.065	151	19	.126
1930-34	85	7	.082	423	17	.040
1935-39	65	1	.015	322	11	.034
1940-44	88	3	.034	443	9	.020
1945-54	311	10	.032	1533	40	.026
		28			110	

These SMR comparisons are in agreement with the preceding relative risk and linear rank analyses; there is no significant difference in mortality, based on these data, between the Ranch Hand group and the comparison group.

3. Noncause Specific Occupational Comparisons

Within-group comparisons by occupation via SMR's, with P-values for testing constant relative risk across year of birth strata (P1) and for testing relative risk equal to unity (P2) are given in Tables 13 through 16. The enlisted and ground personnel are the internal standards in these comparisons. Comparisons via the logrank procedure are given in Table 17.

Table 13

RANCH HAND OFFICERS VERSUS RANCH HAND ENLISTED
MORTALITY BY YEAR OF BIRTH
(SMR = .544; P1=.280, P2= .087)

Birth Year	Ranch Hand Officers			Ranch Hand Enlisted		
	At risk	Dead	Rate	At Risk	Dead	Rate
1905-24	41	3	.073	29	6	.207
1925-34	194	4	.021	194	13	.067
1935-39	93	4	.043	114	3	.026
1940-44	90	2	.022	118	3	.025
1945-54	45	2	.044	329	10	.030
		15			35	

Table 14

RANCH HAND FLYING PERSONNEL VERSUS RANCH HAND GROUND PERSONNEL
MORTALITY BY YEAR OF BIRTH
(SMR = .581; P1=.382, P2=.100)

Birth Year	Ranch Hand Fliers			Ranch Hand Ground		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-24	44	4	.091	26	5	.192
1925-34	272	8	.029	116	9	.078
1935-39	142	6	.042	65	1	.015
1940-44	120	2	.017	88	3	.034
1945-54	63	2	.032	311	10	.032
		22			28	

Table 15

COMPARISON GROUP OFFICERS VERSUS COMPARISON GROUP ENLISTED
MORTALITY BY YEAR OF BIRTH
(SMR = .697; P1=.640, P2=.015)

Birth Year	Comparison Officers			Comparison Enlisted		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-19	44	4	.091	66	9	.136
1920-24	161	13	.081	80	11	.138
1925-29	290	18	.062	211	22	.104
1930-34	640	31	.048	749	36	.048
1935-39	458	11	.024	562	22	.039
1940-44	495	6	.012	601	17	.028
1945-54	190	5	.026	1624	45	.028
		88			162	

Table 16

COMPARISON FLYING PERSONNEL VERSUS COMPARISON GROUND
MORTALITY BY YEAR OF BIRTH
(SMR = .930; P1=.305, P2=.867)

Birth Year	Comparison Fliers			Comparison Ground		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-19	45	6	.133	65	7	.108
1920-24	175	17	.097	66	7	.106
1925-29	350	21	.060	151	19	.126
1930-34	966	50	.052	423	17	.040
1935-39	698	22	.032	322	11	.034
1940-44	653	14	.021	443	9	.020
1945-54	276	10	.036	1538	40	.026
		140			110	

Table 17

LOGRANK WITHIN GROUP COMPARISONS

Comparison	Logrank	P-Value
RH Officer vs RH Enlisted	-1.468	0.142
RH Flyers vs RH Ground	-1.455	0.146
Comparison Officer vs Comp Enlisted	-2.597	0.009
Comparison Flyers vs Comp Ground	-0.363	0.717

The SMR and logrank analyses are somewhat in agreement, with both procedures finding significant differences between comparison officers and comparison enlisted, with the officers living longer. The two methods approximately agree on the Ranch Hand fliers versus ground personnel and on Ranch Hand officer versus enlisted personnel with the logrank result near significance at the .10 level; the fliers appear to be living longer than the ground personnel within the Ranch Hand group.

4. Cause Specific Ranch Hand Versus Comparison Mortality

Cause specific mortality, relative risks, two-sided P-values for testing relative risk equal to unity, power and 95% confidence intervals for relative risks are summarized in Table 18 for the 1241 matched Ranch Handers and their mortality comparisons. Mortality data for the six unmatched Ranch Handers were not used in this analysis. Of the six, one has died of an accident and the rest are still alive. In some categories, the data were too sparse for relative risk estimation.

Table 18

CAUSE SPECIFIC MORTALITY AND RELATIVE RISKS

	Dead		Relative			
Cause	RH	Comparison	Risk	95% Conf Int.	P-value	Power
Accidental	18	92	.959	(.466 - 1.453)	.875	.047
Suicide	3	14	1.071	(0 - 2.407)	.913	.061
Homicide	2	3	3.333	(0 - 9.297)	.099	.489
Infectious, Parasitic	0	3				
Malignant Neoplasm	4	39	.503	(0 - 1.024)	.205	.153
Uncertain Neoplasm	0	2				
Endocrine	1	1	5.000	(0 -18.859)	.102	.562
Mental Disorder	0	1				
Nervous System	0	2				
Circulatory	16	70	1.002	(.411 - 1.594)	.994	.050
Respiratory	0	4				
Digestive	5	11	2.273	(0 - 4.675)	.085	.457
Genitourinary	0	3				
Ill Defined	0	2				
Unknown	0	3				
	49	250				

The low powers in Table 18 reflect the sparseness of data or the fact that some of the observed relative risks approach unity. However, two categories do stand out as deserving further attention: malignant neoplasms and digestive system deaths. It should be noted that if matched sets are ignored and relative risk is estimated using the method of Mantel and Haenszel (14), these results remain essentially unchanged; using this approach, the relative risk for malignant neoplasms, for example, is .506 with a P-value of .195 and power equal to .254. The 95% confidence interval for relative risk using this approach is .180 to 1.419. The Mantel-Haenszel relative risk for the digestive system comparison is 2.254, with a P-value of .132 and a power equal to .325; the 95% confidence interval for relative risk is .782 to 6.501. The digestive system deaths are further defined in Table 19. There has been an increase in deaths due to liver disease among the Ranch Handers; however, this observed difference is not statistically significant. These data are also based on death certificate diagnoses and will be subjected to verification and validation from medical record and autopsy reports. When all deaths from liver disease are considered as a whole, a relative risk of 2.50 is found, with a 95% confidence interval of 0 to 5.501. The P value is 0.083. Similarly, the relative risk for pancreatitis is 2.50 with a 95% confidence interval of 0 to 8.501.; the P value is 0.386. These observations are of interest and will be pursued in depth in subsequent reports.

Table 19

DIGESTIVE SYSTEM MORTALITY

ICD Code (9th Ed)	Deaths	
	Ranch Hand	Comparison
Pancreatitis (5770)	1	2
Alcoholic cirrhosis (5712)	0	3
Nonalcoholic cirrhosis (5715)	3	3
Nonalcoholic fatty liver (5718)	0	1
Chronic liver disease (5728)	0	1
Alcoholic liver disease (5711)	1	0
Duodenal ulcer (5325)	0	1
	5	11

Table 20

SITE SPECIFIC MALIGNANT NEOPLASM MORTALITY

Site ICD Code (9th Ed)	Deaths	
	Ranch Hand	Comparison
Lip, oral cavity, Pharynx (140-149)	0	4
Digestive organs, peritoneum (150-159)	0	8
Respiratory, intrathoracic (160-165)	2	15
Bone, connective tissue, skin, breast (170-175)	0	1
Genitourinary organs (179-189)	1	3
Brain (191-192)	0	3
Lymphatic and hematopoietic tissue (200-208)	0	4
No site specification (199)	1	1
	4	39

The malignant neoplasms are detailed in Table 20, the cell types of the neoplasms, as recorded on the death certificates, are summarized in Table 21.

Table 21

MORPHOLOGY OF NEOPLASMS

ICD Code 9th Ed.	Nomenclature	Deaths	
		Ranch Hand	Comparison
M800	Neoplasms not otherwise specified (NOS)		
	Brain	0	1
	Bronchus and Lung	0	3
	Colon	0	1
	Intestinal Tract	0	1
M801-804	Epithelial neoplasms (NOS)		
	Bronchus and Lung	1	8
	Esophagus	0	1
	Kidney	1	1
	Nasopharynx	0	1
	Pancreas	0	2
	Unspecified site	1	1
M805-808	Papillary and Squamous Cell		
	Nasal Sinus	0	1
	Lip	0	1
	Tongue	0	1
	Tonsil	0	1
M814-838	Andenomas and Adenocarcinomas		
	Appendix	0	1
	Bronchus and Lung	0	2
	Colon	0	1
	Kidney	0	2
	Stomach	0	1
M872-879	Nevi and Melanomas		
	Skin (NOS)	0	1
	Mediastinal	1	0
M905	Mesothelioma		
	Bronchus and Lung	0	1
M938-948	Gliomas		
	Frontal Lobe	0	1
	Brain (NOS)	0	1
M959-963	Lymphomas NOS and Diffuse		
	Lymphomas (NOS)	0	1
M965-966	Hodgkins disease		
	Hodgkin's (NOS)	0	2
M986	Myeloid Leukemias		
	Acute Myelocytic Leukemia	0	1
		4	39

Epithelial, papillary and adenomas account for 64% of the comparison neoplasms. Three Ranch Hand neoplasms arose from epithelial cells. There were no tumors in either group which were classified as soft tissue sarcoma.

Chapter IV

NONCAUSE SPECIFIC COMPARISONS WITH EXTERNAL POPULATIONS

1. Background and Motivation

It is important to know, not only how the Ranch Handers and their matched comparisons relate to each other, but also how they compare with general military and male United States populations. Pitfalls inherent in these comparisons are well known and are briefly reviewed below for specific comparisons with 1978 DoD period life tables for nondisability retired military officer and enlisted personnel (15) and the 1978 U.S. White Male Life Table (16). Although there are difficulties in the use of these comparisons, their use does provide an additional indicator of trends in mortality when viewed in the context of the total analytic process.

2. Adjustment Difficulties

Mortality rates in any military population are strongly dependent upon 1) calendar year of death, 2) military status (active duty, separated, retired), 3) selection and retention, and 4) branch of service. Adjustment for these effects was not made in these comparisons because published select Air Force life tables, by calendar year and by status, are not available. In addition, there is also a problem with the statistical method used, since the Gail and Ware (17) procedure assumes constant relative risk with respect to age; the selection effect has been shown to diminish sharply with time making this assumption untenable in these comparisons. The adjustment difficulties (1-4), and their likely consequences, are detailed below. These difficulties apply to all of the comparison groups, but these concerns have less effect on the comparisons of the Ranch Hand group to their matched cohort since these two groups are generally equivalent, relative to these key factors.

A. Adjustment for Calendar Year of Death

Due to the continuing decrease in overall mortality in the military (18) and in the United States (19), the referenced external age-specific rates are appropriate only for the calendar period of the referenced external life table, that is, 1977-79 for the 1978 period military table used in this analysis. The 1977-79 period rates would, for example, be too low for comparison with subjects dying in 1970 at the age of 40. These subjects would more properly be compared with the death rate for 40 year olds in a 1970 period life table or with a death rate for 40 year olds in a cohort military life table for subjects born in 1930. Calendar time is not taken into account in this analysis because period life tables covering the three decades from 1950 to 1980, for the the active duty, separated and retired Air Force subpopulations, are not currently available. This discrepancy is serious because the decline in death rates in the active duty Air Force during the period 1966 to 1980 has been very substantial (18).

B. Adjustment for Military Status (Active Duty, Separated, Retired).

The only published military life tables available at this writing are 1978 period tables for DoD nondisability retired officer and enlisted personnel (15) and a series of yearly abridged tables for the active duty Air Force, the first covering the period 1966-1968 and the last, 1978-1980 (18). With these data limitations, adjustment for military status is not possible. It is

clear, however, that there are substantial differences between active duty and retired death rates with the active duty rates being lower than retired rates (15).

C. Adjustment for Selection

Entry into the military carries with it an effect known as selection, a lengthening of life expectancy due to health prerequisites upon entry into select status and periodic health checks thereafter. This effect is well known to insurance actuaries who have observed that, in insured populations, the effect diminishes as time passes unless there are continued checks on the state of health of the insured persons (20). If selection is to be adjusted for in this analysis, it would be necessary to know Air Force death rates as a function of both age and of time elapsed since entry into the Air Force. It would also be necessary, therefore, to know enlistment and discharge or retirement dates for all study subjects. It is the lack of these data that makes this adjustment impossible at this time. The consequences of this lack of adjustment are not known at this writing.

D. Adjustment for Branch of Service

Age specific active duty Air Force death rates are substantially lower than the corresponding rates for other services (18). Nonservice specific death rates are therefore too high for appropriate comparison with these two study groups.

3. Comparisons with 1978 DoD Life Tables

In Tables 22 and 23, Ranch Hand officers and comparison group officers are contrasted to a 1978 DoD nondisability retired officer life table (15) and in Tables 24 and 25, Ranch Hand and comparison group enlisted personnel are compared with a 1978 DoD nondisability retired enlisted life table (15). In each table, the column labeled "At Risk" lists the number of subjects entering each five year age interval, the column labeled "Deaths" tabulates the numbers of deaths in the age intervals and the column labeled "Expected Deaths" gives the expected numbers of deaths in the age intervals if the study subjects had experienced the same death rates as those specified by the DoD table. The value of the test statistic (17) for testing the null hypothesis of equality is denoted by T; its two-sided P-value is denoted by P. While each table summarizes the findings with five year age intervals for ease of presentation, one year age intervals were used for the computation of the statistic T. All comparisons are conditioned on survival to age 35, since the DoD tables begin at that age. All comparisons are unadjusted for race since the DoD tables are not race specific.

Table 22

RANCH HAND OFFICER VERSUS DOD NONDISABILITY
RETIRED OFFICER LIFE TABLE
(T = -3.962, P < .001)

Age	At Risk	Deaths	Expected Deaths
35-39	456	2	4.183
40-44	366	1	4.244
45-49	288	1	4.578
50-54	173	1	3.099
55-59	57	1	2.043
60-64	30	2	.823
65-68	1	0	.076
		8	19.046

Table 23

COMPARISON OFFICERS VERSUS DOD NONDISABILITY
RETIRED OFFICER LIFE TABLE
(T = -2.402, P = .016)

Age	At Risk	Deaths	Expected Deaths
35-39	2264	12	20.837
40-44	1822	13	20.703
45-49	1365	24	21.920
50-54	842	12	15.901
55-59	308	9	10.265
60-64	145	4	4.377
65-68	19	0	.601
		74	94.604

Table 24

ENLISTED RANCH HANDERS VERSUS DOD NONDISABILITY
RETIRED ENLISTED LIFE TABLE
(T = -.239, P = .811)

Age	At Risk	Deaths	Expected Deaths
35-39	668	6	6.748
40-44	392	5	5.601
45-49	287	5	6.326
50-54	140	5	4.154
55-59	41	2	2.203
60-64	20	2	1.484
65-69	6	0	.576
70-71	1	1	.096
		26	27.188

Table 25

ENLISTED COMPARISON SUBJECTS VERSUS DOD NONDISABILITY
RETIRED ENLISTED LIFE TABLE
(T = -3.214, P = .001)

Age	At Risk	Deaths	Expected Deaths
35-39	3299	21	33.370
40-44	1945	20	27.681
45-49	1437	31	31.450
50-54	695	14	20.076
55-59	203	12	10.980
60-64	103	3	7.515
65-59	35	1	2.593
70-74	5	0	.646
		102	134.311

These findings suggest that, if the effects discussed in section 2 are assumed to be negligible, Ranch Hand officers and comparison officers and comparison enlisted personnel are living longer than expected relative to their respective external populations. Enlisted Ranch Hand personnel are not different from DoD enlisted personnel. In the above DoD comparison there is a suggestion of interaction between officer-enlisted categories and Ranch Hand versus comparison group membership. If matching and time of death are ignored, the following table can be constructed. The term "rate" is as defined on page 8 of this report.

Table 26

DEATH AFTER 35 YEARS

	Ranch Hand			Comparison		
	Alive	Dead	Rate	Alive	Dead	Rate
Officer	448	8	.018	2190	74	.033
Enlisted	642	26	.039	3197	102	.031

Analysis using log-linear models shows a statistically significant interaction with $p \leq 0.05$. It appears that Ranch Hand officers have a lower mortality after age 35 than Ranch Hand enlisted or comparison officers or enlisted. However, the converse situation is noted considering mortality prior to age 35 and is significant with $p \leq 0.05$. The data for this analysis of mortality prior to age 35 is set out below.

Table 27

DEATHS BEFORE AGE 35 YEAR

	Ranch Hand			Comparison		
	Alive	Dead	Rate	Alive	Dead	Rate
Officer	456	7	.015	2264	14	.006
Enlisted	775	9	.011	3833	60	.015

These interactions will require further detailed analysis and evaluation, with specific consideration of medical covariables including risk taking, other life patterns and herbicide.

4. Comparisons with U.S. 1978 White Male Life Table

Non-Black Ranch Handers and non-Black comparisons are compared in this section with the population of White males, as represented by the 1978 U.S. White Male Life Table (16). Two serious and well known problems with the use of this table are the lack of adjustments for the calendar year and selection effects just described; when comparing occupational cohorts with national populations, the selection effect is known as the "healthy worker" effect. The pitfalls of these kinds of comparisons are well documented (21, 22, 23). In Tables 28 and 29, non-Black Ranch Handers and non-Black comparisons are compared, via the method of Gail and Ware (17), with the 1978 U.S. White Male Life Table (16). In Tables 30 through 33, non-Black officers and enlisted personnel in both study groups are compared with the same 1978 U.S. White Male Table.

Table 28

NON-BLACK RANCH HANDERS VERSUS 1978 U.S. WHITE MALE LIFE TABLE
(T=-4.588, P <.001)

Age	At Risk	Deaths	Expected Deaths
21-24	1171	2	9.003
25-29	1169	6	9.783
30-34	1163	7	9.396
35-39	1054	7	9.256
40-44	722	5	10.381
45-49	549	6	12.085
50-54	304	5	8.114
55-59	98	3	5.039
60-64	50	4	2.790
65-69	7	0	0.669
70-71	1	1	0.089
		46	76.605

Table 29

NON-BLACK COMPARISONS VERSUS THE 1978 U.S. WHITE MALE LIFE TABLE
(T = -11.230, P <.001)

Age	At Risk	Deaths	Expected Death
19-19	5816	1	10.325
20-24	5815	16	55.444
25-29	5799	27	48.592
30-34	5772	23	46.719
35-39	5245	31	46.124
40-44	3593	29	51.041
45-49	2675	50	58.810
50-54	1487	26	40.529
55-59	509	20	25.210
60-64	248	7	14.461
65-69	54	1	3.403
70-74	5	0	0.601
		231	354.540

Table 30

NON-BLACK RANCH HAND OFFICERS VERSUS 1978 U.S. WHITE MALE LIFE TABLE
(T = -4.575, P < .001)

Age	At Risk	Deaths	Expected Deaths
25-29	454	3	3.794
30-34	451	4	3.710
35-39	447	2	4.420
40-44	362	1	5.304
45-49	285	1	6.370
50-54	172	1	4.541
55-59	57	1	3.019
60-64	30	2	1.302
65-68	1	0	0.110
		15	32.570

Table 31

NON-BLACK COMPARISON OFFICERS VERSUS 1978 U.S. WHITE MALE
LIFE TABLE
(T = -7.923, P < .001)

Age	At Risk	Deaths	Expected Deaths
25-29	2253	9	18.880
30-34	2244	5	18.530
35-39	2239	12	22.137
40-44	1801	13	25.841
45-49	1352	24	30.468
50-54	834	12	23.328
55-59	308	9	15.157
60-64	145	4	6.923
65-68	19	0	0.887
		88	162.151

Table 32

NON-BLACK RANCH HAND ENLISTED PERSONNEL VERSUS 1978 U.S. WHITE MALE
LIFE TABLE
(T = -1.753, P = .080)

Age	At Risk	Deaths	Expected Deaths
21-24	717	2	5.510
25-29	715	3	5.988
30-34	712	3	5.686
35-39	607	5	4.836
40-44	360	4	5.077
45-49	264	5	5.716
50-54	132	4	3.573
55-59	41	2	2.020
60-64	20	2	1.488
65-69	6	0	0.588
70-71	1	1	0.089
		33	40.571

Table 33

NON-BLACK COMPARISON ENLISTED PERSONNEL VERSUS THE 1978 U.S. WHITE MALE LIFE TABLE
(T =-5.923, P < .001)

Age	At Risk	Deaths	Expected Death
19-19	3563	1	6.325
20-24	3562	16	33.938
25-29	3546	18	29.713
30-34	3528	18	28.189
35-39	3006	19	23.987
40-44	1792	16	25.200
45-49	1323	26	28.341
50-54	653	14	17.201
55-59	201	11	10.053
60-64	103	3	7.538
65-69	35	1	2.515
70-74	5	0	0.601
		143	213.601

Given the cautions just described, these findings suggest that the non-Black Ranch Handers and comparisons are living much longer than expected relative to the 1978 U.S. White Male Life Table. The ratios of the observed to the expected deaths described in Tables 28 and 29 reveal that the Ranch Hand and comparison subjects are experiencing death at only 60 to 65% of the rate of the U.S. White male population. The ratio is 0.461 for the subset of Ranch Hand officers, 0.543 for comparison officers, 0.813 for enlisted Ranch Handers, and 0.669 for enlisted comparison subjects. The healthy worker effect is very likely a major contributor to the undoubtedly real differences between these study groups and the general population.

Chapter V

COMPARISONS WITH THE WEST POINT STUDY GROUP

1. Background and Motivation

The statistical and epidemiological literature is replete with warnings against the uncritical use of the SMR and related summary measures for comparing study groups with published vital statistics for national populations or subpopulations (5), (24), (25). Those cautions are based on the adjustment difficulties described in Chapter 4, Section 2, and departures from the assumption of constant relative risk across age intervals between the study group and the external population. These drawbacks can be avoided by not referencing an external standard at all, by using one of the study groups as the standard (13), or by using as an external standard a group of military personnel, born during approximately the same years, with the same mortality follow-up, as the Ranch Hand and comparison groups.

An external group of sufficient size for meaningful statistical comparisons is not available at this time. Mortality and year of birth data are available, however, on a small group of West Point graduates, the subjects of the West Point Follow-up Study. Although this group is too small for all but very crude statistical comparisons (1), it is the only known external data available at this time. The following comparisons are, therefore, primarily descriptive.

The West Point Study Group consists of 474 members of the West Point graduation class of 1956. These men have been followed up since then for morbidity and mortality. All members of that class were, or still are, officers in the U.S. Armed Forces. The purpose of the West Point study is to investigate the relationship between blood lipid levels and cardiovascular disease. Each study subject is physically examined biennially and blood samples are obtained for lipid and lipoprotein analyses at the USAF School of Aerospace Medicine (26).

2. Noncause Specific Comparisons of Ranch Hand and Comparison Subgroups with the West Point Study Group

For the purpose of these mortality comparisons, 15 of the 36 known West Point deaths occurring on or before 31 December 1982 were deleted, 9 of the 15 were killed in action, one was killed in 1959 in the line of duty and 5 were killed in automobile crashes prior to 1962. These deletions imitate the deletion of personnel killed in action from the Ranch Hand and comparison groups. Noncombat or accidental deaths prior to 1962 were deleted because death prior to 1962 would have precluded membership in the Ranch Hand or comparison groups. In addition, one West Pointer who is also a Ranch Hander, was deleted; that individual was alive on 31 December 1982.

A summary of the remaining 21 deaths among the 458 West Point subjects used in these analyses is given by year of birth in Table 34 and by age in Table 35. In Table 35 the column headed "censored" lists by age, the number of West Pointers alive on 31 December 1982.

Table 34

WEST POINT DEATHS BY YEAR OF BIRTH

Year of Birth	At Risk	Dead
1930	20	0
1931	59	2
1932	90	6
1933	136	8
1934	141	4
1935	12	1
	458	21

Table 35

WEST POINT DEATHS BY AGE

Age	At Risk	Censored	Dead
25-29	458	0	2
30-34	456	0	5
35-39	451	0	3
40-44	448	0	2
45-49	446	276	8
50-52	162	161	1
		437	21

In this analysis, non-Black Ranch Hand and comparison officers are compared, without regard to cause of death, with the West Point study group; all of the West Point subjects are non-Black. Non-Black Ranch Hand Officers were matched, one-to-one, by year of birth, to West Point subjects. Due to the relatively small number of Ranch Hand officers and the limited year of birth range imposed by the age of the Class of 1956, only 283 of the 458 West Point subjects received a matched Ranch Hander. Matched sets with West Pointers having the same year of birth were then merged to create six matched sets, corresponding to the six years of birth, 1930 through 35, of the West Pointers. To compare West Pointers with comparison officers, two non-Black comparison officers were matched to each West Pointer by year of birth. All West Pointers received two matched comparison individuals. Matched sets with West Pointers having the same year of birth were merged, giving six matched sets containing a total of 916 comparisons.

Logrank tests were carried out on these two matched data sets, and the results are summarized in Table 36. In these analyses, survival time is age at death. Censorship is due to survival to 31 December 1982. For those still alive on 31 December 1982, censoring time is age on that day.

Table 36

STUDY GROUP VERSUS WEST POINT GROUP
LOGRANK COMPARISONS WITH TWO-SIDED P-VALUES

Comparison	P-Value
Ranch Hand officer versus West Point	.218
Comparison officer versus West Point	.528

An SMR analysis, with the West Pointers being the standard, is summarized in Table 37.

Table 37

SMR COMPARISON OF NON-BLACK RANCH HAND AND COMPARISON OFFICERS WITH THE WEST POINT STUDY GROUP

	(SMR = .530)			(SMR = .778)			(SMR = 1)		
Birth	Ranch Hand			Comparison			West Point		
Year	At Risk	Dead	Rate	At Risk	Dead	Rate	At Risk	Dead	Rate
25-31	95	2	.021	272	19	.070	79	2	.025
32	35	1	.029	164	7	.043	90	6	.067
33-34	60	1	.017	257	6	.023	277	12	.043
35-40	93	4	.043	223	5	.022	12	1	.083
		8			37			21	

The test for constant relative risk across year of birth strata gives a P-value of .229. Further, a likelihood ratio test suggests that these SMR's are not different (P = .392).

32-911 O—84——15

3. Cause Specific Comparisons

The cause specific death counts for the West Point Study Group are given in Table 38.

Table 38
WEST POINT MORTALITY BY CAUSE

Cause	Count
Accidents	6
Infectious disease	1
Malignant neoplasms	6
Circulatory	5
Digestive	1
Genitourinary	1
Ill defined	1
	21

Cause specific comparisons are carried out with three causes, cancer (malignant neoplasms), other diseases, and nondisease (accidents, suicides, homicides and ill-defined), with an adjustment for year of birth by stratification on year of birth. Relative risks are calculated using the method of Mantel and Haenszel (14). These results, based on the counts in Tables 39 and 40, are shown in Table 41.

Table 39

CAUSE SPECIFIC COMPARISONS
RANCH HAND OFFICERS VERSUS WEST POINT

Cause	Birth Year	Ranch Hand		West Point	
		At Risk	Dead	At Risk	Dead
Nondisease	1925-1933	166	1	305	5
	1934-1940	117	4	153	1
Cancer	1925-1930	72	0	20	0
	1931	23	0	59	1
	1932	35	0	90	3
	1933	36	0	136	1
	1934	24	0	141	1
	1935-1940	93	0	12	0
Other diseases	1925-1934	190	2	446	8
	1935-1940	93	1	12	1

Table 40

CAUSE SPECIFIC COMPARISON
COMPARISON OFFICERS VERSUS WEST POINT

Cause	Birth Year	Comparisons		West Point	
		Number	Dead	Number	Dead
Nondisease	1929-1931	272	11	79	1
	1932	164	2	90	2
	1933	148	1	136	2
	1934-1937	332	2	153	1
Cancer	1929-1931	272	2	79	1
	1932	164	2	90	3
	1933	148	1	136	1
	1934-1937	332	2	153	1
Other diseases	1929-1932	436	9	169	1
	1933	148	1	136	5
	1934	109	1	141	2
	1935-1937	223	3	12	1

Table 41

CAUSE SPECIFIC RELATIVE RISKS, P-VALUES
95% CONFIDENCE INTERVALS FOR LOG RELATIVE RISK

Cause	Comparison	RR	95% Conf Interval for Log Rel Risk	P-value	Power
Nondisease	RH vs WP	1.072	(-1.504 - 1.643)	.931	.051
	Comp vs WP	0.841	(-1.354 - 1.009)	.775	.059
Cancer	RH vs WP				
	Comp vs WP	0.690	(-1.634 - .891)	.564	.089
Other diseases	RH vs WP	0.474	(-3.540 - 2.047)	.600	.082
	Comp vs WP	0.779	(-2.367 - 1.867)	.817	.056
All causes	RH vs WP	0.539	(-2.191 - .954)	.441	.120
	Comp vs WP	0.728	(-1.940 - .306)	.702	.067

While the Ranch Hand versus West Point cancer comparison cannot be assessed using the Mantel-Haenszel procedure, the absence of Ranch Hand cancer deaths in this analysis is of interest. This finding is consistent with the apparent but nonsignificantly decreased Ranch Hand cancer mortality noted in the Ranch Hand versus matched comparison group analysis (Chapter III).

Chapter VI

STATISTICAL ASPECTS

1. Purpose

The purposes of this chapter are 1) to briefly describe each statistical procedure used in the preceding chapters 2) to state the underlying assumptions of each procedure and 3) discuss the validity of those assumptions in this study. The procedures used in this analysis were survival curve estimates and confidence bands, linear rank tests, relative risk estimation and standardized mortality ratios. Points 1-3 are addressed for each procedure in Sections 2 through 5.

2. Survival Curve Estimation and Confidence Bands

The survival function of a homogeneous population, S(t), is defined as the probability of surviving t years. The problem is to estimate S(t) and make a confidence statement about that estimate based on randomly censored data. Randomly censored data occur in survival studies since analyses are usually carried out before all subjects have failed. In the present application, failure is defined as death and censorship occurs because most subjects are still living at the time of analysis. Other causes for censorship in this kind of epidemiological study are loss to follow-up or death from causes other than those of interest. Thus far in this study, there have been no subjects lost to follow-up, and all causes of death are of interest.

The survival function is estimated here by the product limit estimate K(t), also called the Kaplan-Meier estimate (6). This estimate is derived under the assumption that, in a life testing experiment with n subjects on test, exactly k subjects, with k less than n, are observed to fail; the other n-k remaining are observed only until they are censored. The subjects are assumed drawn randomly from a homogeneous population. Censorship is assumed to be independent of failure. The Kaplan-Meier estimator is asymptotically unbiased and reduces to one minus the empirical distribution function in the absence of censoring.

In the present application, the homogeneous populations are the Ranch Handers, the comparisons and various subgroups of these two groups. Death time is taken as age at death measured to the nearest month; censoring time is age on 31 December 1982, measured to the nearest month. Survival time is age at death or age on 31 December 1982 for those subjects still living.

The process $n[K(t)-S(t)]$ converges weakly to a zero mean Gaussian process, as n tends to infinity, under random censorship when the underlying survival function S(t) and the censoring distribution are continuous on a bounded interval (27). This convergence is the theoretical basis for the confidence band algorithm (7) used in Figures 2 and 3, Chapter III and Appendices VI.

The independence of death and censorship can be assumed to hold here since censorship (survival to December 31, 1982) is not being invoked on individuals because they appear to be at unusually high, or low, risk of death (28). Direct contact has been lost with two Ranch Handers and nine comparisons as described in Chapter II, but these are assumed to be alive, and hence censored at their age on 31 December 1982. The reason for this assumption is that the extensive death ascertainment system is believed to be thorough enough so that, had any of these subjects died, the death would have been detected. Hence, while contact has been lost, loss to follow-up for the purpose of mortality determination has not occurred (29). All other subjects still alive on 31 December 1982 are censored at their age on that date.

The validity of inferences based on the estimate K(t) and its associated confidence band depends on the sample size and the observed number of deaths. The sample sizes and numbers of deaths in every stratum used in these analyses exceed the minimum requirements for these procedures (7).

The survival curve estimates and confidence bands displayed in Figures 2 and 3 and Appendix VI are not adjusted for year of birth. To do so would have required stratification on year of birth, creating many small strata with associated sample size difficulties. Some year-of-birth adjusted plots in the larger occupational strata will be presented in the next report.

3. Linear Rank Procedures

The hypothesis of interest in this analysis is that the actual survival distributions of the Ranch Handers and their matched comparisons are identical. The procedures of choice for testing equality of the two unknown survival distributions based on the matched and censored data in this study are the censored data extensions of the exponential scores and Wilcoxon tests, due to Prentice (8). The first of these is widely known as the logrank test. The test statistics, T, are of the form given by equation 6-23 of (28), where the summands are calculated on matched sets consisting of survival information on one Ranch Hander and his matched mortality comparisons. The statistic T, for either logrank or generalized Wilcoxon summands, is approximately standard normal under the null hypothesis (9).

The large sample normal approximation for T will hold when all distributions are continuous and all censoring times are mutually independent of each other and independent of death. These assumptions are well satisfied in this study since the censorship mechanism, survival to time of analysis, does not favor one group over the other.

In these procedures, the sampling unit is a matched set, so that these tests are adjusted for all matching variables. Prior to calculation, matched sets with Ranch Handers in the same race and job classification having the same year of birth are merged.

The logrank and extended Wilcoxon tests are locally most powerful when the logarithm of the survival times are distributed as extreme value or logistic random variates, respectively. While the efficiency of these procedures peaks at these two underlying distributions, they have been shown to be robust against departures (8). These distributional assumptions, however, are not viewed as strictly valid in this study since there is good evidence in the literature that survival time due to certain cancers and other diseases is log normally distributed (30, 31, 32, 33). A linear rank procedure of the Prentice form, whose efficiency peaks under the lognormal distributional assumption, can be constructed (34), but this algorithm is not available at the present time; it will be included in the next analysis. The effect of this departure from the assumptions is considered mild. It should also be noted that these distributional assumptions cannot be checked since these match sets are small and the observations in the combined samples of all matched sets cannot be assumed to have a common distribution. Therefore, reliance must be placed on historical data to determine which linear rank procedure to use. The logrank and Wilcoxon procedures are used here because they are powerful and widely accepted in epidemiology and statistics.

4. Relative Risk Estimation

Two relative risk estimators are used in this analysis, a generalization of the Ejigou-McHugh estimator for one to many matched data (12) and the Mantel-Haenszel estimator for stratified data (14). The Ejigou-McHugh estimate was chosen because it allows full adjustment for the one-to-many year-of-birth matching in this study, it is asymptotically as efficient as the maximum likelihood estimator and it is noniterative. The Mantel-Haenszel estimate was chosen because of its ease of calculation, efficiency (35), and general acceptance. It's variance is estimated according to the advice of Anderson et al. (36). Recent work suggests that the variance of the Mantel-Haenszel statistic might be better estimated by a jack-knife procedure (37); this newer method will be carried out in the next mortality report.

The Ejigou-McHugh estimator in its published form is suitable only for 1 to R matched designs in which the number, R, of controls matched to each case is the same for all cases. Since the number of controls matched to each Ranch Hander is not the same for all Ranch Handers, the Ejigou-McHugh estimate and its variance was extended to a one-to-many matched design in which the number of comparisons is allowed to vary from case to case. Since this extension is unpublished it is stated in Appendix V for reference.

The extended estimate and its variance reduces to the Ejigou-McHugh estimate and variance when all matched sets contain an equal number of comparisons. It is asymptotically efficient and consistent and is noniterative.

The Ejigou-McHugh estimate and the Mantel-Haenszel estimate are based on the assumption that relative risk is constant across levels of the matching variable. Some indication that this assumption holds in this study when the data is grouped, by stratifying on year of birth, is furnished by likelihood ratio testing; there is no evidence in this study to suggest that relative

risk is not constant across levels of the matching variables when the event of interest is death from any cause. Therefore, the Ejigou-McHugh and Mantel-Haenszel estimates are appropriate for these data.

5. Indirect Standardization

With either an external or internal standard, the SMR is a good summary mortality index for comparing two or more populations, provided the product model, $P_{ij}=r_i p_j$, holds, where P_{ij} is the probability of death in stratum i of population j, r_i is a set of standard stratum specific rates and p_j characterizes the mortality of population j, i=1,2, ..., I, j=1,2, ..., J, (38, 13). If standard rates are known from some external source and if the product model holds, the best estimate of p_j is proportional to the SMR. If J=2, the product model holds, and if one of the two groups is used as the standard, the SMR estimates relative risk. In any case, any SMR summary of mortality data should be preceded by analytical and graphical tests of fit of the product model. Because one of the study groups was always used as the standard in these analyses, the test of fit of the product model was, equivalently, a test of constancy of relative risk across year of birth strata. The fit of the model was verified in each analysis. Further, a likelihood ratio test for equality of population was carried out as described by Gail (13). The results of both tests are summarized by their P-values in each application. The sample sizes in every application are large enough so that chi-square approximations hold; these analyses are, therefore, valid and appropriate.

The expected number of deaths in the SMR used in these analyses was calculated as $\sum n_{ij}r_i$, where n_{ij} is the number of subjects in the ith stratum of the jth population. The person-years SMR was not used here for two reasons. First, its validity as an estimator of relative risk is dependent upon the fit of the proportional hazards model for which an omnibus test is not currently available. Secondly, the person-years calculation is typically carried out from entry into follow-up (5); in this study, follow-up begins at first entry to Vietnam or Southeast Asia and these entry dates are being verified at this writing.

6. Comparing Observed Life Table Data with a Known Survival Curve

The procedure of Gail and Ware (17) is used in these analyses to compare Ranch Hand and comparison group survival data with published period life tables. The basic assumptions of this procedure are that death and censorship are independent competing risks and that the reference curve is a survival distribution for some external population. The test is of the form $\sum(o_j-e_j)/(\sum v_j)^{1/2}$, where o_j and e_j are observed and expected numbers of deaths in age interval j, and v_j is the variance of o_j-e_j. The statistic is not an omnibus goodness-of-fit test consistent against all alternatives to the null hypothesis that the observed sample comes from a known survival distribution. Rather, it has good power against proportional hazards alternatives or, more loosely, against alternatives for which the observed survival is better (or worse) in every interval than predicted by the known survival curve.

The independence of death and censorship assumption is well satisfied in these data, as discussed in Section 2 of this chapter. The life tables used in these analyses do not, however, represent the survival distribution of any population since they are period, not cohort, life tables. The appropriateness of this procedure is, therefore, dependent upon the extent to which these period life tables approximate the survival distribution of some relevant reference population. These period tables were used because the more appropriate cohort life tables were not available at the time of analysis.

Chapter VII

CONCLUSION

1. Introduction

The mortality analyses described in this report have not revealed any adverse death experience in the herbicide/dioxin exposed cohort. The results of the analyses, regardless of the source of the comparison data were consistent: at this time, there is no indication that operation Ranch Hand personnel have experienced any increased mortality or any unusual patterns of death in time or by cause. They are not dying in increased numbers, at earlier ages, or by unexpected causes.

The fact that only a relatively small number of Ranch Hand deaths were available for analysis is reassuring in itself. However, the fact that adverse effects have not yet been detected does not imply that an effect will not become manifest at a future time or after covariate adjusted analyses. For this reason, further analyses are intended and mortality in the study population will be ascertained annually for the next 20 years.

A summary of the statistical techniques applied to each source of comparison data is presented in Table 42. It should be noted here that these analyses have been carried out without knowledge of covariate information, such as herbicide exposure, industrial chemical exposure, or other risk factors and that these analyses were carried out at a time when approximately 96% of Ranch Handers and their matched comparison subjects were still living. The data, therefore, must be viewed as preliminary to more definitive analyses, which will be performed over the next 20 years. Table 43 summarizes the results of the noncause specific analyses by source of the comparison data, and Table 44 presents the results of the cause specific analyses.

Table 42

SUMMARY OF STATISTICAL PROCEDURES USED IN ANALYSIS

Comparison Database	Internal Comparison Group	1978 U.S. White Males	1978 DoD Life Tables	West Point Class of 1956
Noncause Specific Analyses				
Logrank & Wilcoxon Procedures	+			+
Ejigou-McHugh Relative Risk	+			
Mantel-Haenszel Relative Risk	+			+
SMR/Breslow-Day Product Model	+			+
Gail-Ware Procedure		+	+	
Cause Specific Analyses				
Ejigou-McHugh Relative Risk	+			
Mantel-Haenszel Relative Risk	+			+

Procedure usage is indicated by a "+" symbol.

SUMMARY OF NONCAUSE SPECIFIC MORTALITY ANALYSES BY SOURCE OF COMPARISON DATA

	Internal Comparison Group	1978 US White Males[1]	1978 DoD Life Tables[1]	West Point Class of 1956[2]
Ranch Hand Group	$RH = C$ $RH_O = C_O$ $RH_E = C_E$ $RH_F = C_F$ $RH_G = C_G$	RH <<<US RH_O <<<US RH_E ≤US	RH_O <<<DoD_O $RH_E = DoD_E$	$RH_O = WP_O$
Comparison Group		C <<<US C_O <<<US C_E <<<US	$C_O < DoD_O$ C_E <<DoD_E	$C_O = WP_O$
Internal Occupational Group Specific	$RH_O \leq RH_E$ $RH_F \leq RH_G$ $C_O < C_E$ $C_F = C_G$			

= P value[3] greater than .10
≤ P value equal to or less than .10
< P value equal to or less than .05
<< P value equal to or less than .01
<<< P value equal to or less than .001

RH Ranch Hand Group
C Comparison Group
O Officers
E Enlisted
F Flying
G Ground

1 Validity of these comparisons is questionable (see Chapter 4)
2 Statistical inference is limited by small sample size
3 All P value symbols are based upon SMR and Gail-Ware analysis

Table 44

SUMMARY OF CAUSE SPECIFIC ANALYSES BY SOURCE OF COMPARISON DATA

RH Versus Internal Comparison	RH Versus West Point*
No significant difference in cause specific relative risks	No significant difference in cause specific relative risks

* Statistical inference is limited by small sample size

2. Internal Comparison Group

Based on these early results, there appears to be no significant difference between Ranch Handers and comparisons as regards mortality. This null finding holds for both cause specific and noncause specific comparisons. One within group comparison did yield a significant difference, however. The non-Black comparison officers are living significantly longer than the non-Black comparison enlisted personnel. This may reflect the underlying health care and socioeconomic differences between these two groups. Non-Black Ranch Hand officers also appear to be living longer than non-Black Ranch Hand enlisted personnel, but this finding cannot be viewed as significant, with a P-value of .142 (Table 17). This lack of significance in the Ranch Hand analysis might be attributed to the smaller group sizes within the Ranch Hand cohort in contrast to the comparison cohort.

3. External Comparisons

As outlined in the study protocol, considerable effort was expended in the selection of the study comparison group. While the chosen comparison group appeared closest to the Ranch Hand cohort except for herbicide exposure, it seemed appropriate to also contrast the Ranch Hand mortality experience to that of additional comparison groups. Three additional comparison data sets were then selected: mortality data from the West Point Class of 1956, the DoD Nondisability Retired Officer and Enlisted Life Tables for 1978, and the U.S. White Male Life Table, also for 1978. These data sets were chosen in a hierarchical fashion with the expectation that, in the absence of a herbicide effect, the Ranch Handers would have: 1) a mortality pattern comparable to the West Pointers, 2) a lower mortality than the DoD group due to the healthy worker effect, and 3) a still lower mortality than the U.S. male cohort due to healthy worker and military selection effects. These expectations were reassuringly fully realized with respect to overall mortality. Additionally, interesting officer-enlisted differentials emerged. As discussed below, these officer-enlisted differentials may have resulted from sample size effects or from covariable effects, potentially including herbicide exposure.

4. Power Considerations

The power limitations of this study, specifically regarding mortality from rare conditions, such as soft tissue sarcoma, were fully acknowledged and described in the protocol (Ref 1, page 67). For example, a fatal disease with an incidence of .001 would require an approximate risk of 4 for a power of 0.8.

Power calculations, while desirable for planning and study design, are also revealing at analysis. They are, however, sometimes difficult to carry out without further assumptions. The powers of the logrank and Wilcoxon tests

and the likelihood ratio tests in the SMR analyses are not calculable at this time due to the lack of appropriate methodology. The powers of the tests for cause specific mortality were calculated at the estimated relative risk. The values were low because the estimates of relative risk were close to unity and/or the data were sparse.

The null findings in this report are unlikely to have been observed by chance had the true group differences been substantial. For example, if the true overall relative risk were in fact equal to 2, a crude calculation gives a probability of .0007 of observing a relative risk smaller than the observed .964 (Table 7). This probability is less than .001 if the true relative risk is 1.5. These findings are, therefore, very likely reflective of a near overall equivalence between Ranch Handers and their matched comparisons. Finally, these unadjusted findings do not preclude the possibility of the emergence of significant differences after adjustment for risk factors.

5. Consistency Patterns

When the analysis of each external comparison data base is considered separately, the restrictions inherent in each source limit the strength of the inferences which can be made. However, when the results of all internal and external comparison data bases are considered in context, some patterns of consistency emerge. While some of these patterns may not have firm statistical underpinnings, they still may provide epidemiologic clues to the dynamics of the mortality process.

The Ranch Hand officers exhibit a very consistent and predictable pattern across all analyses. As shown in Table 43, their mortality is nearly the same as that of their most equivalent comparison groups (the matched comparison group officers and the West Point group). As the comparison groups become progressively less equivalent to the Ranch Hand group, the relative mortality of the Ranch Hand officers improves, presumably due to selection comparability (healthy worker effect, etc.). Their mortality is lower than that of their enlisted counterparts; however, this difference is not as striking as is the statistically significant comparable analysis between the matched comparison officers and the matched enlisted personnel.

Unfortunately, the cross-comparison trends for the enlisted Ranch Handers are not as clearcut. Their mortality is greater,though not significantly different from their matched comparisons. The enlisted comparison group had a highly significant underrepresentation of mortality against both the DoD and US life tables, whereas the Ranch Handers are equivalent to the DoD group and only marginally better than the 1978 US White males.

The consistent observation that the enlisted Ranch Handers appear to demonstrate less of a difference in relative mortality than do their matched comparisons is intriguing. This may reflect an actual increase in mortality due to herbicide exposure or some other factor, or it could be an artifact of small sample size created by the 1:5 matching or basic comparability problems as previously described. The inclusion of substantially more subjects in one group than another can have a profound effect on the significance level of a

statistical technique. Nevertheless, these observations are of interest, and will continue to be subjected to detailed analysis throughout the course of the follow-up study. This trend is consistent with self-perception of herbicide exposure held by many of the Ranch Hand group. Covariate analyses will be conducted, the herbicide exposure index will be applied to these data, and the effects of interaction will be assessed to determine whether the Ranch Hand enlisted findings are real or artifactual.

The next mortality assessment will include analyses by person-year of follow-up, adjusted for age in an effort to better address the issue of latency. As the number of deaths in the study population increases with the passage of time, all of the statistical approaches outlined in the protocol (1) will be applied to the data.

Appendix I

RANCH HAND II PRINCIPAL INVESTIGATORS
COINVESTIGATORS, CONTRIBUTORS, AND MANAGEMENT PERSONNEL

A. Principal Investigators

George D. Lathrop, MD, MPH, PhD, FACPM
Colonel, USAF,MC
Chief, Epidemiology Division

Patricia M. Moynahan, RN, MS
Colonel, USAF, NC
Chief, Occupational Epidemiology Section

Richard A. Albanese, MD, GM-15
Chief, Biomathematical Modeling Branch
Data Sciences Division

William H. Wolfe, MD, MPH, FACPM
Lt Colonel, USAF,MC
Chief, Epidemiology Services Branch

B. Coinvestigators

Joel E. Michalek, PhD, GS-13
Mathematical Statistician
Data Sciences Division

Richard C. McNee, MS, GM-13
Chief, Advanced Analysis Branch
Data Sciences Division

Alton J. Rahe, MS, GS-13
Mathematical Statistician
Data Sciences Division

Appendix I (Continued)

C. Contributors

William J. Besich, BS, GS-12
Computer Systems Analyst
Data Sciences Division

Vincent V. Elequin, BS, RRA, GS-11
Medical Record Librarian
Occupational Epidemiology Section

William E. Nixon, BS, GM-13
Computer Systems Analyst
Data Sciences Division

Thomas J. White, MA
Senior Subject Matter Specialist
Data Sciences Division

Alvin L. Young, BS, MS, PhD
Major, USAF
Special Assistant in Military Herbicides

D. Management Personnel

Project Director:

Roy L. DeHart, MD, MPH, MS, FACPM
Colonel, USAF, MC
Commander, USAF School of Aerospace Medicine

Project Resource Manager:

Melvin B. Dobbs
Colonel, USAF, BSC
Director, Systems Acquisition Research, Development and Acquisition
Aerospace Medical Division

Air Force HQ Systems Command Coordinator:

Ronald D. Burnett
Colonel, USAF, BSC
Command Bioenvironmental Engineer
Office of the Command Surgeon

Air Force Surgeon General Coordinator:

Robert A. Capell
Major, USAF, BSC
Assistant for Bioenvironmental Engineering
Office of the Surgeon General

32-911 O—84——16

Appendix II

SCIENCE PANEL

Advisory Committee on Special Studies Relating to the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants.

Dr. G. W. Comstock
Johns Hopkins Research Center
Box 2067
Hagerstown MD 21740

Dr. John Doull
Professor
Department of Pharmacology and Toxicology
University of Kansas Medical Center
Kansas City KA 66103

Dr. John A. Moore (Chair)
Deputy Director
National Toxicology Program
P.O. Box 12233
Research Triangle Park NC 27709

Dr. Richard Monson
Professor of Epidemiology
Harvard School of Public Health
677 Huntington Avenue
Boston MA 02115

Dr. Norton Nelson
Professor and Chairman
Department of Environmental Medicine
New York University
School of Medicine
New York NY 10016

Dr. Alan Poland
Associate Professor of Oncology
McCardle Laboratory
University of Wisconsin
Madison WI 53706

Dr. Irving Selikoff
Director, Environmental Sciences Laboratory
Mt Sinai School of Medicine
5th Avenue and 100th Street
New York NY 10029

Appendix III

MATCHING RESULTS IN THE MORTALITY POPULATION

The matching results are described here for the mortality population consisting of 1241 Ranch Hands, their 6171 matched mortality comparisons, and the six unmatched Ranch Hands. The matching procedure is described in the Protocol (Ref. 1, pages 23-26).

All study subjects were matched perfectly on job category. Three mismatches occurred on race because the recorded race designations for three study subjects were found to be incorrect at the LHA interview. These three subjects were comparisons, two were in the enlisted-other stratum (one was originally recorded as Black and was discovered to be non-Black, the other was originally recorded as non-Black and was discovered to be Black), and one was in the enlisted-flight engineer stratum (he was originally recorded as Black and was discovered to be non-Black).

Matching on date of birth was carried out by first expressing date of birth in months from 1 January 1900, to the nearest month; the result is termed month-of-birth. Six discrepancies occurred in matching on month-of-birth due to erroneous months-of-birth for one Ranch Hand and one comparison. These were discovered at the LHA interview. The Ranch Hand, in the non-Black enlisted-other stratum, was discovered to be 72 months older than was recorded prior to the matching. The comparison, in the non-Black officer-pilot stratum, was found to be 15 years younger than was originally recorded. The erroneous Ranch Hand month-of-birth put all five of his matched comparisons 12 months out of range since he was originally perfectly matched to all five mortality comparisons. The erroneous comparison month-of-birth put that comparison 119 months out of range. Given the very small number of mismatches on age and race relative to the number of subjects, their effect was assumed negligible.

The matching by month-of-birth, overall, and within each of the ten job and race categories within the mortality population is summarized in this Appendix. The column headed "Age Difference" lists absolute differences of months-of-birth of Ranch Hands and comparisons. The column headed "Number of Comparisons with RH younger (older)" gives, at each level of age difference, the number of comparisons within the level of age difference and older (younger) than the Ranch Hand to whom they are matched. The column headed "Total Count" gives the total numbers of comparisons having the absolute age differences with their matched Ranch Hand given in the first column; in "Total Percent", these counts are expressed as percentages of 6171. These are cumulated in the last two columns.

Appendix III

MATCH SUMMARY FOR THE MORTALITY POPULATION

Strata	Age Difference	Number of Comparisons with RH		Total		Cumulative	
		Younger	Older	Count	%	Total	%
Overall	0			4261	69.0	4261	69.0
	1-6	743	706	1449	23.5	5710	92.5
	7-12	77	102	179	2.9	5889	95.4
	13-18	40	36	76	1.2	5965	96.7
	19-24	22	22	44	0.7	6009	97.4
	25-30	12	19	31	0.5	6040	97.9
	31-36	16	14	30	0.5	6070	98.4
	37-42	10	19	29	0.5	6099	98.8
	43-48	9	13	22	0.4	6121	99.2
	49-54	13	7	20	0.3	6141	99.5
	55-60	17	7	24	0.4	6165	99.9
	72	0	5	5	0.1	6170	100.0
	179	0	1	1	0.0	6171	100.0
Officer-pilot	0			961	55.2	961	55.2
Non-Black	1-6	272	259	531	30.5	1492	85.8
	7-12	33	32	65	3.7	1557	89.5
	13-18	20	17	37	2.1	1594	91.6
	19-24	8	12	20	1.1	1614	92.8
	25-30	9	11	20	1.1	1634	93.9
	31-36	13	10	23	1.3	1657	95.2
	37-42	7	18	25	1.4	1682	96.7
	43-48	7	11	18	1.0	1700	97.7
	49-54	11	7	18	1.0	1718	98.7
	55-60	14	7	21	1.2	1739	99.9
	179	0	1	1	0.1	1740	100.0
Officer-Pilot	0			0	0.0	0	0.0
Black	1-6	3	0	3	23.1	3	23.1
	7-12	3	0	3	23.1	6	46.2
	31-36	0	1	1	7.7	7	53.9
	37-42	2	0	2	15.4	9	69.2
	43-48	1	0	1	7.7	10	76.9
	49-54	2	0	2	15.4	12	92.3
	55	1	0	1	7.7	13	100.0
Officer-	0			240	61.5	240	61.5
Navigator	1-6	74	70	144	36.9	384	98.5
Non-Black	7-12	0	6	6	1.5	390	100.0

Appendix III (Continued)
MATCH SUMMARY FOR THE MORTALITY POPULATION

Strata	Age Difference	Number of Comparisons with RH		Total		Cumulative	
		Younger	Older	Count	%	Total	%
Officer-Navigator Black	0			1	10.0	1	10.0
	1-6	0	1	1	10.0	2	20.0
	7-12	2	2	4	40.0	6	60.0
	13-18	0	1	1	10.0	7	70.0
	19-24	0	1	1	10.0	8	80.0
	25-30	0	1	1	10.0	9	90.0
	31-36	0	1	1	10.0	10	100.0
Officer-Other Non-Black	0			14	11.4	14	11.4
	1-6	38	57	95	77.2	109	88.6
	7-12	2	8	10	8.1	119	96.8
	13-18	1	1	2	1.6	121	98.4
	19-24	1	0	1	0.8	122	99.2
	25	0	1	1	0.8	123	100.0
Officer-Other Black	13-18	2	0	2	100.0	2	100.0
Enlisted-Flight Engineer Non-Black	0			516	55.2	516	55.2
	1-6	165	141	306	32.7	822	87.9
	7-12	29	34	63	6.7	885	94.7
	13-18	16	14	30	3.2	915	97.9
	19-24	0	7	7	0.7	922	98.6
	25-30	2	6	8	0.9	930	99.5
	31-36	2	1	3	0.3	933	99.8
	37-42	1	0	1	0.1	934	99.9
	46	1	0	1	0.1	935	100.0
Enlisted-Flight Engineer Black	0			10	13.3	10	13.3
	1-6	26	22	48	64.0	58	77.3
	7-12	7	5	12	16.0	70	93.3
	19-24	3	0	3	4.0	73	97.3
	55-58	2	0	2	2.7	75	100.0
Enlisted-Other Non-Black	0			2382	90.6	2382	90.6
	1-6	116	91	207	7.9	2589	98.5
	7-12	1	11	12	0.5	2601	99.0
	13-18	1	3	4	0.2	2605	99.1
	19-24	10	2	12	0.5	2617	99.6
	25-30	1	0	1	0.0	2618	99.6
	31-36	1	1	2	0.1	2620	99.7
	37-42	0	1	1	0.0	2621	99.7
	43-48	0	2	2	0.1	2623	99.8
	72	0	5	5	0.2	2628	100.0
Enlisted-Other Black	0			137	53.7	137	53.7
	1-6	49	65	114	44.7	251	98.4
	7-12	0	4	4	1.6	255	100.0

Appendix IV

YEAR OF BIRTH, OCCUPATIONAL AND RACE SPECIFIC MORTALITY

Job Category, Race	Birth Year	Ranch Hand At Risk	Ranch Hand Dead	Ranch Hand Death Rate	Comparison At Risk	Comparison Dead	Comparison Death Rate
Officer-Pilot, Non-Black	1915-19	8	3	.375	39	4	.103
	1920-24	31	0		155	13	.084
	1925-29	31	0		232	14	.060
	1930-34	113	3	.027	456	23	.050
	1935-39	66	3	.045	326	8	.025
	1940-44	60	1	.017	354	5	.014
	1945-49	40	2	.050	178	5	.028
	TOTAL	349	12	.034	1740	72	.041
Officer-Pilot, Black	1930-34	0	0		3	0	
	1935-39	1	0		4	0	
	1940-44	3	0		6	0	
	1945-49	2	0		0	0	
	TOTAL	6	0		13	0	
Officer-Navigator Non-Black	1925-29	9	0		47	3	.064
	1930-34	35	1	.029	163	7	.043
	1935-39	21	1	.048	105	3	.029
	1940-44	13	0		67	0	
	1945-49	2	0		8	0	
	TOTAL	80	2	.025	390	13	.033
Officer-Navigator Black	1930-34	1	0		6	0	
	1935-39	1	0		4	0	
	TOTAL	2	0		10	0	
Officer-Other, Non-Black	1910-14	1	0		2	0	
	1915-19	0	0		3	0	
	1920-24	1	0		6	0	
	1925-29	3	0		11	1	.091
	1930-34	2	0		12	1	.083
	1935-39	4	0		19	0	
	1940-44	13	1	.077	66	1	.015
	1945-49	1	0		4	0	
	TOTAL	25	1	.040	123	3	.024

Appendix IV (Continued)

Job Category, Race	Birth Year	Ranch Hand At Risk	Ranch Hand Dead	Death Rate	Comparison At Risk	Comparison Dead	Death Rate
Officer-Other, Black	1940-44	1	0		2	0	
	TOTAL	1	0		2	0	
Enlisted-Flt Eng Non-Black	1915-19	1	1	1.000	6	2	.333
	1920-24	4	0		20	4	.200
	1925-29	12	0		61	3	.049
	1930-34	64	3	.047	304	15	.049
	1935-39	48	2	.042	243	10	.041
	1940-44	41	0		211	7	.033
	1945-49	19	0		90	5	.056
	TOTAL	189	6	.032	935	46	.049
Enlisted-Flt Eng Black	1925-29	1	0		10	1	.100
	1930-34	6	1	.167	34	5	.150
	1935-39	5	0		16	1	.063
	1940-44	3	1	.333	15	2	.133
	TOTAL	15	2	.133	75	9	.120
Enlisted-Other Non-Black	1905- 9	0	0		2	0	
	1910-14	4	2	.500	10	2	.200
	1915-19	8	0		48	5	.104
	1920-24	12	3	.250	60	7	.117
	1925-29	28	2	.071	140	18	.129
	1930-34	76	6	.079	376	14	.037
	1935-39	52	1	.019	263	8	.030
	1940-44	67	2	.030	340	7	.021
	1945-49	270	9	.033	1333	36	.027
	1950-54	11	0		56	0	
	TOTAL	528	25	.047	2628	97	.037
Enlisted-Other Black	1930-34	7	1	.143	35	2	.057
	1935-39	9	0		40	3	.075
	1940-44	7	0		35	1	.029
	1945-49	29	1	.034	145	4	.028
	TOTAL	52	2	.038	255	10	.039

Appendix V

THE EXTENDED EJIGOU-McHUGH RELATIVE RISK ESTIMATOR

Let R_k, k=1,2, ..., K, denote the distinct numbers of comparisons matched to the cases and let n_k denote the number of matched sets with exactly R_k comparisons. A matched set is defined as the case and his matched comparisons. Let $n=n_1+n_2+ \ldots +n_K$ denote the total number of matched sets.

Define $Z_{k,i,T}$, k=1,2, ...,K, i=0,1, by

$Z_{k,0,T}$ = the number of matched sets, among those having exactly R_k comparisons, in which the case is alive and exactly T of the R_k comparisons have died, T=1,2, ..., R_k

$Z_{k,1,T}$ = the number of matched sets, among those having exactly R_k comparisons in which the case has died and exactly T of the R_k comparisons have died, T=0,1,2, ..., R_k-1.

The extended estimate, ψ, is given by

$$\psi = \frac{\sum_{k=1}^{K}\sum_{T=1}^{R_k} Z_{k,0,T}Z_{k,1,T-1}/(Z_{k,0,T}+Z_{k,1,T-1})}{\sum_{k=1}^{K}\sum_{T=1}^{R_k} TZ^2_{k,0,T}/(R_k-T+1)(Z_{k,0,T}+Z_{k,1,T-1})}$$

and its variance is estimated by

$$\sigma^2 = \frac{\psi}{\sum_{k=1}^{K}\sum_{T=1}^{R_k} Z_{k,0,T}/[\psi+(R_k-T+1)/T]}.$$

Since K is finite, this estimate has the same distributional properties as the Ejigou-McHugh estimator; it is asymptotically efficient and unbiased. The underlying assumptions used in its derivation are that the disease under study is of low incidence and that relative risk is constant over the levels of the matching variables. The Ejigou-McHugh estimate and the above extension are equivalent in asymptotic efficiency to maximum likelihood estimation (12).

Appendix VI

Figure 4
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR POOLED RANCH HANDERS

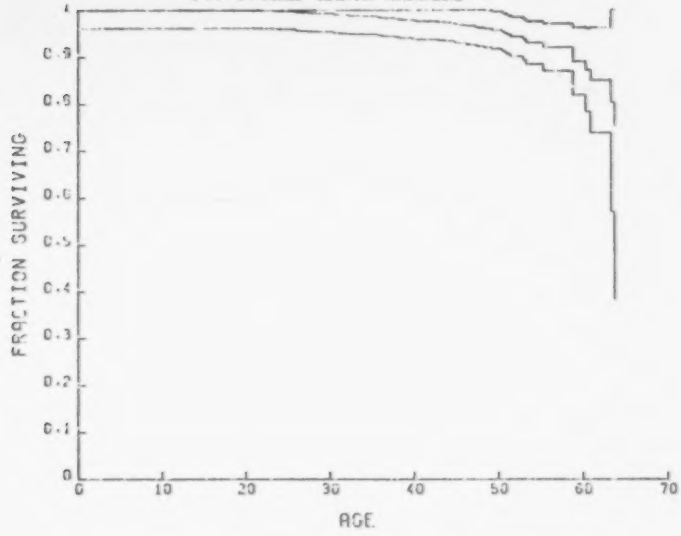


Figure 5
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR POOLED COMPARISONS

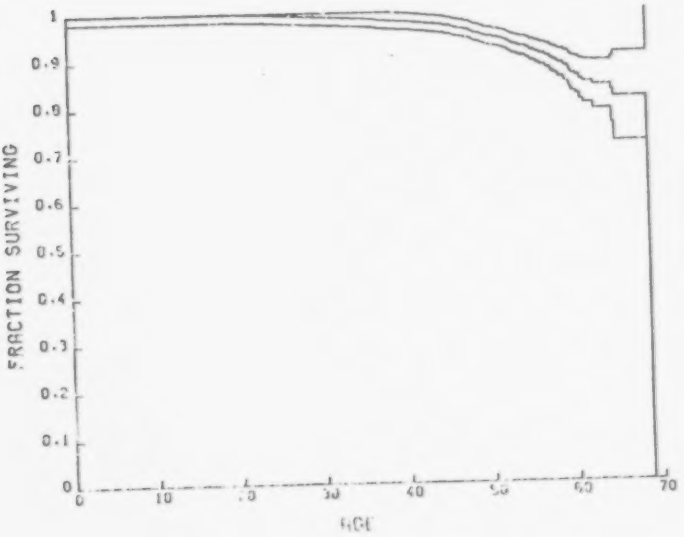


Figure 6
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR RANCH HAND OFFICERS

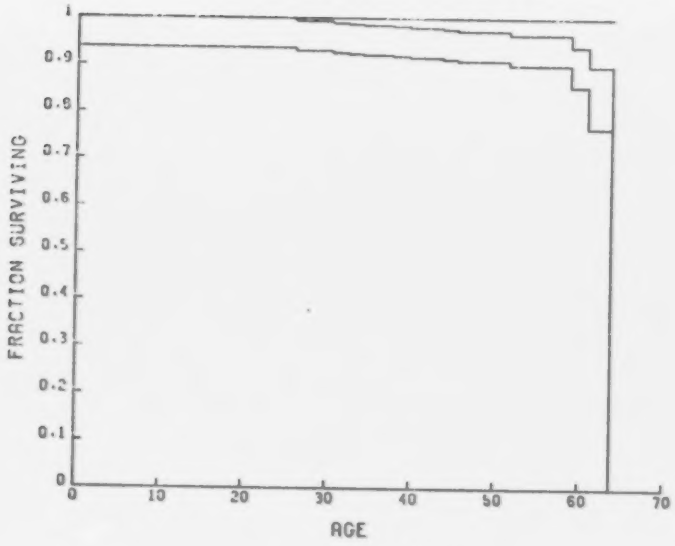


Figure 7
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR COMPARISON OFFICERS

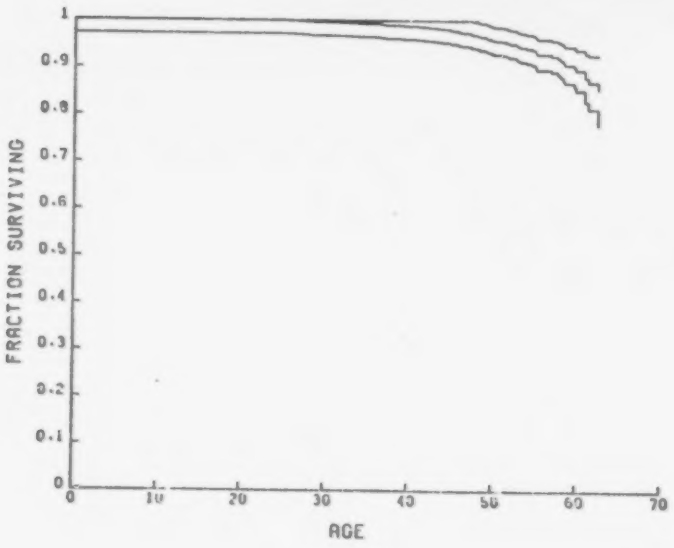


Figure 8
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR RANCH HAND ENLISTED PERSONNEL

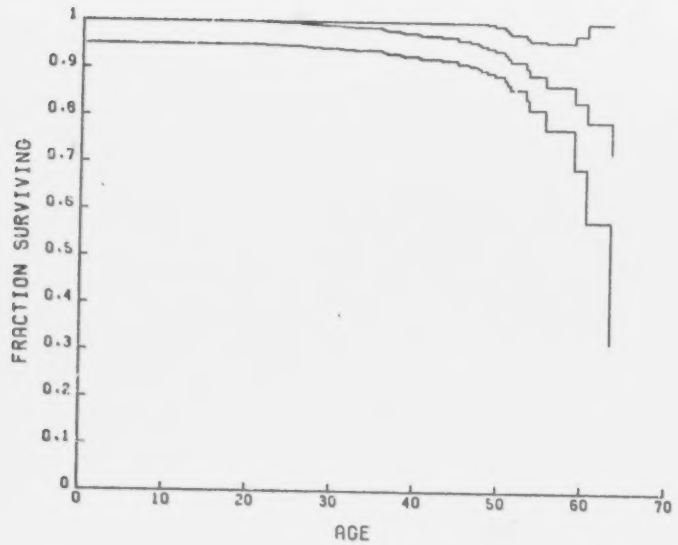


Figure 9
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR COMPARISON ENLISTED PERSONNEL

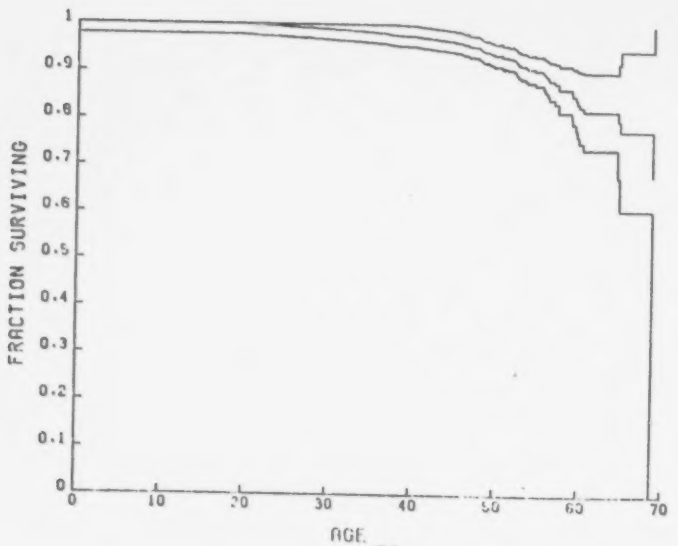


Figure 10
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR RANCH HAND FLYING PERSONNEL

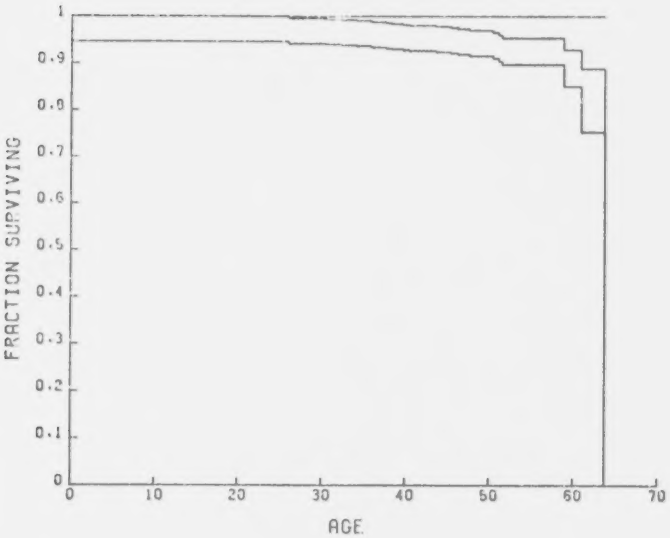


Figure 11
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR COMPARISON FLYING PERSONNEL

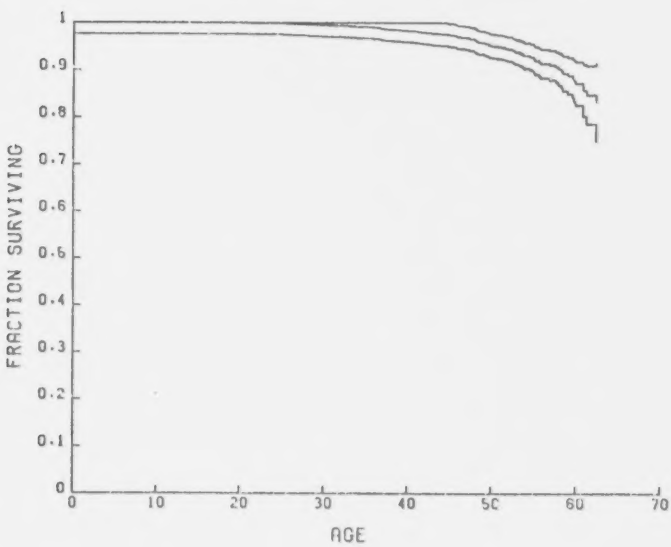


Figure 12

SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR RANCH HAND GROUND PERSONNEL

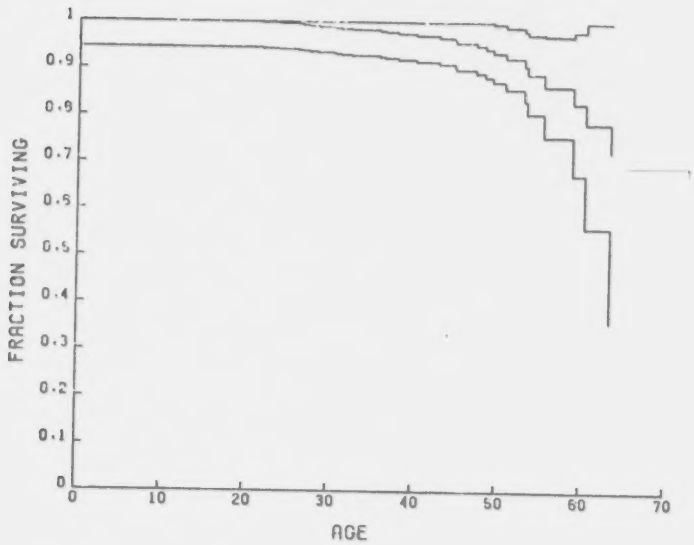
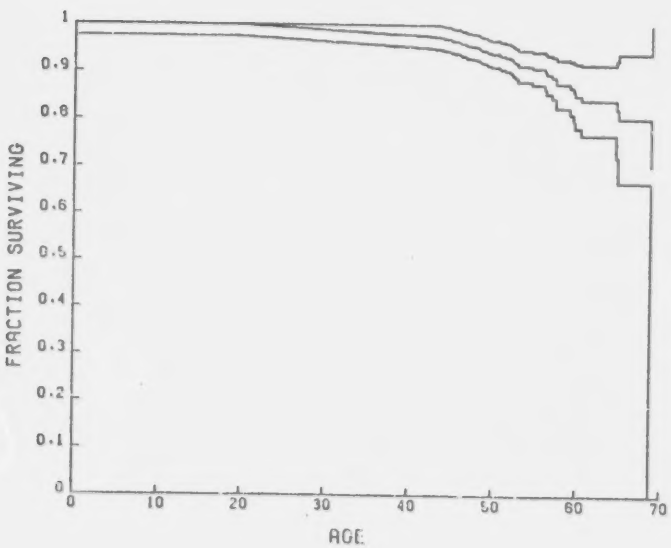


Figure 13

SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR COMPARISON GROUND PERSONNEL



REFERENCES

1. Lathrop, G. D., Wolfe, W. H., Albanese, R.A. and Moynahan, P. M. Epidemiological investigation of health effects in Air Force personnel following exposure to herbicides: Study Protocol. SAM-TR-82-44, Dec 1982.

2. Honchar, P. A., and Halperin, W. E. 2,4,5-T, trichlorophenol, and soft tissue sarcoma. Lancet Jan 31:268-269 (1981).

3. Hardell, L., and Sandstrom, A. Case-control study: soft tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Br. J. Cancer 39:711-717 (1979).

4. Eriksson, M., Hardell, L., Berg, N. O., Moller, T., and Axelson, O. Case-control study on malignant mesenchymol tumors of the soft tissue and exposure to chemical substances. Lakartidningen 76:3872-75 (1979).

5. Breslow, N. E., Lubin, J. H., Marek, P. and Langholz, B. Multiplicative models for cohort analysis. Journal of the American Statistical Association 78:1-12 (1983).

6. Kaplan, E. L. and Meier, P. Nonparametric estimation from incomplete observation. J. Am. Stat. Assoc. 53:457-481 (1958).

7. Hall, W. J. and Wellner, J. A. Confidence bands for a survival curve from censored data. Biometrika 67:133-143 (1980).

8. Prentice, R. L. Linear rank tests with right censored data. Biometrika 65:167-179, (1978).

9. Michalek, J. E. and Mihalko, D. Linear rank procedures for matched observations. SAM-TR-83-16 (In Press), May 1983.

10. Michalek, J. E. and Mihalko, D. Matched survival analysis (MSURV). SAM-TR-83-15 (In Press), May 1983.

11. Michalek, J. E. and Mihalko, D. Linear rank procedures for litter matched data. Biometrics (to appear).

12. Ejigou, A. and McHugh, R. Relative risk estimation under multiple matching. Biometrika 68:85-91 (1981).

13. Gail, M. The analysis of heterogeneity for indirect standardized mortality ratios. Journal of the Royal Statistical Society, Series A 141:224-234 (1978).

14. Mantel, N. and Haenszel, W. Statistical aspects of the analysis of data from retrospective studies of disease. Journal of the National Cancer Institute 22:719-748 (1959).

15. Valuation of the Military Retirement System FY 1980. Office of the Actuary, Defense Manpower Data Center, 300 North Washington Street, Alexandria, Virginia 22314.

16. Vital Statistics of the United States, 1978 Vol II - Section 5, Life Tables; U.S. Dept of Health and Human Services, DHHS Publication No (PHS) 81-1104; Hyattsville, Maryland:1980.

17. Gail, M. H. and Ware, J. H. Comparing observed life table data with a known survival curve in the presence of random censorship. Biometrics 35:285-391 (1979).

18. Annual Report, 1966-1981, Servicemen's Group Life Insurance Program, Insurance Service, Department of Veterans Benefits, Veterans Administration.

19. Cohort Mortality and Survivorship: United States Death-Registration States, 1900-1968. Public Health Service. DHEW Publication No (HSM) 73-1400.

20. Elandt-Johnson, R.C. and Johnson, M.L. Survival Models and Analysis New York: John Wiley, 1980.

21. McMichael, A. J., Standardized Mortality Ratios and the "Healthy Worker Effect": Scratching Beneath the Surface. J. of Occupational Medicine, Vol 18, No. 3, March 1976.

22. Tabershaw, I. R., Special Communications, "What Do We Expect from an Occupational Cohort?", J. of Occupational Medicine, Vol 17, No. 2, February 1975.

23. Enterline, P. E. ; Pitfalls in Epidemiological Research; J. of Occupational Medicine, Vol 18, No. 3, March 1976

24. Gaffey, W. R. A critique of the standardized mortality ratio. Journal of Occupational Medicine 18:157-160 (1976).

25. Wong, O. Further criticisms of epidemiological methods in occupations studies. Journal of Occupational Medicine 19:220-222.

26. Clark, D., Allen, M. and Wilson, F. Longitudinal study of serum lipids-twelve year report. American Journal of Nutrition 20:743-752 (1967).

27. Breslow, N. and Crowley, J. A large sample study of the life table and product limit estimates under random censorship. The Annals of Statistics 2:437-453 (1974).

28. Kalbfleisch, J. D. and Prentice, R. L. The Statistical Analysis of Failure Time Data. New York: John Wiley, 1980.

29. Monson, R. R. Occupational Epidemiology, CRC Press, Inc., Boca Raton FL (1980).

30. Feinleib, M. A method of analyzing log-normally distributed survival data with incomplete follow up. Journal of the American Statistical cal Association 55:534-535 (1960).

31. Feinleib, M. and McMahon, B. Variation in the duration of survival of patients with chronic leukemias. Blood 15:332-349 (1960).

32. Nice, C. M. and Stenstrom, K. W. Irradiation therapy in Hodgkins disease. Radiology 62:641-652 (1954).

33. Osgood, E. E. Methods for analyzing survival data, illustrated by Hodgkin's disease. American Journal of Medicine 24:40-47 (1958).

34. Mehrotra, K. G., Michalek, J. E., Mihalko, D. and White, T. Score computation for linear rank procedures. Journal of Statistical Computation and Simulation 16:201-211 (1982).

35. Breslow, N. Odds ratio estimators when the data are sparse. Biometrika 68:73-84 (1981).

36. Anderson, S., Auquier, A., Hauck, W., Oakes, D., Vandaele, W., and Weisberg, H. Statistical methods for comparative studies, techniques for bias reduction. New York: John Wiley, 1980.

37. Breslow, N. E. and Liang, K. Y. The variance of the Mantel-Haenszel estimator. Biometrics 38:943-952 (1982).

38. Breslow, N. E. and Day, N. W. Indirect standardization and multiplicative models for rates, with reference to the age adjustment of cancer incidence and relative frequency data. Journal of Chronic Diseases 28: 289-303 (1975).